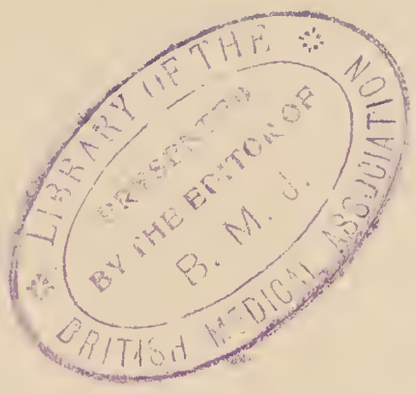
# ON ACUTE INTESTINAL TOXÆMIA IN INFANTS

*RALPH VINCENT*

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## AN EXPERIMENTAL INVESTIGATION OF THE ETIOLOGY AND PATHOLOGY OF EPIDEMIC OR SUMMER DIARRHŒA

BY

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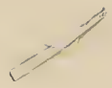


# ON ACUTE INTESTINAL TOXÆMIA IN INFANTS

Mr. President, Ladies and Gentlemen,

I cannot enter upon my subject without expressing my sense of the honour conferred upon me by you, Sir, and the Council of this Society, in inviting me to address you.

When I received the invitation I was somewhat fearful of the responsibilities its acceptance involved. But I could not deny myself the pleasure of responding to the generous compliment you had paid me, and forthwith I took thought as to the subject of my address. I was not long in coming to a decision. For several years the disease in infants officially termed "Epidemic Diarrhœa" has been the subject of my constant study, while during the whole of the present year I have been actively investigating its etiology day by day, and, I might also say, night by night. I felt that the best response to your invitation would be to offer the results to your Society on this occasion.

My next duty—an equally pleasant one—is to make my acknowledgments to my friend and colleague, Mr. Robert Mond, Treasurer of the Infants Hospital. Not only did he build and equip the hospital where

the clinical observations which led to the present investigations were made, but he has entirely maintained at his own expense its research laboratory. But for the hospital he built and the laboratory he maintains, this paper could not have been written.

The experiments on the animals involved the provision of extensive and special accommodation. It would have been extremely difficult, if not impossible, for me to have carried out this part of the research had it not been for the hospitality extended to me by the Governing Body of the Lister Institute. To them, and to Dr. C. J. Martin, the Director of the Institute, I desire to express my sincere thanks for the courtesy and consideration extended to me.

# I

## On Certain General Considerations

Milk of the purest character contains in all normal circumstances a variety of micro-organisms. Pathogenic organisms are never present under normal conditions, and when present, have gained access to the milk by transference from the products of disease in the cow or in those handling the milk. In this paper I deal with organisms which are always present in milk, and which under normal conditions are not pathogenic.

These organisms fall into two very distinct classes —those that produce acid in milk and those that do not. The first class of organisms is not very commonly found, apart from milk. When plates are exposed to the air in different places and under varied conditions, numerous organisms, some pathogenic and many not pathogenic, are found. But the acid-producing organisms always present in milk are very seldom to be found on plates exposed to the air, unless the plates have been exposed in places where milk is constantly being handled. Even in these circumstances the colonies that arise from the acid-producing organisms are comparatively few in number.

These organisms are, however, invariably found in one situation—namely, in the more superficial portions of the udder of the cow. The milk in the mammary

gland is sterile, but the outermost parts of the ducts leading to the exterior always contain bacteria, and those organisms producing lactic acid in milk are, relatively, abundant.

Thus, by a process of natural selection, not difficult to understand, the organisms most readily developing in milk are so placed that they come into contact with their typical food at the earliest moment—namely, at the moment the cow is milked. Nevertheless, the number of organisms reaching the milk in this manner is very limited when compared with the number of other organisms that are found in it when the handling of the milk is conducted in an insanitary manner. In these circumstances it will be found that the number of non-lactic organisms is greatly in excess of the lactic organisms. But if this milk be kept for a few hours at or about incubator temperature, it will be found that the lactic organisms have established an enormous preponderance, for these have rapidly developed in the milk, while the others have remained inert and have made no increase upon their original number.

For most of the adventitious organisms reaching the milk are quite unable to grow in an acid medium, and the production of acidity by the lactic organisms prevents their development in, and their action upon, milk. Hence the discrimination between these two groups of organisms is not an arbitrary one, but is essentially related to the relative functions of these organisms and their behaviour in milk.

It is not without interest in this connection to compare the composition of cow's milk with that of human milk. In cow's milk the fat, lactose, and albuminoids

are present in nearly equal proportions—fat, 4 per cent. ; lactose, 4·50 per cent. ; albuminoids, 3·50 per cent. In human milk the proportions are very different. Lactose constitutes more than one-half of the total solids. It is nearly twice as much as the fat and more than three times as much as the albuminoids. The susceptibility of the human infant to intestinal affections is compensated for by the presence in its natural food of an exceptional amount of lactose.

The essential distinction between the two classes of organisms may be illustrated by a single experiment. On March 9, 1910, a sample of milk (fat-free) was taken from the milk laboratory of the Infants Hospital. It was divided into two portions, A and B. B was placed in a flask, sealed with cotton-wool, and was then boiled for two minutes. A, in its raw condition, was put into a bottle and corked. Both were then incubated at 85° F. (29·4° C.). In thirty-six hours the raw milk had curdled, and the reaction was strongly acid. In seventy-two hours the boiled milk had curdled, but the reaction was amphoteric—*i.e.*, precisely the same as that of the pure milk when fresh.[1] In the boiled specimen (B) the curd gradually dissolved till in the course of about a week the flask contained a rather viscid brownish-yellow fluid. The raw milk, however, underwent no further change.

Although in both instances coagulation of the proteins occurred, this coagulation was of a very different character. Caseinogen is coagulated by a

[1] Cow's milk is almost invariably acid. When fresh from the cow it is amphoteric. The milk in use at the Infants Hospital is amphoteric, owing to its refrigeration at the farm and its protection during transit by means of insulated churns.

very small amount of acid. A few drops of dilute acetic acid is sufficient to precipitate the curd in milk. This coagulation is, therefore, merely an incidental feature. The essential feature is the action of the lactic organisms. As a result of their action the lactose is decomposed, lactic acid being the final result. The reaction is shown in the following equation :

$$\underset{\text{Lactose.}}{C_{12}H_{22}O_{11}} + H_2O = 4\underset{\text{Lactic acid.}}{C_3H_6O_3}.$$

In regard to the boiled specimen, such an explanation of the curdling is entirely inadmissible, for there was no production of acid. The result of the boiling is that the lactic organisms are killed, and as they do not possess spores, the agents of the lactic fermentation are entirely destroyed. The putrefactive bacteria are also killed by the boiling, but their spores are uninjured. In consequence, the only organisms developing in the milk after the boiling are those which arise from the spores of the putrefactive bacteria. These organisms act, not on the milk-sugar, nor on the fat, but entirely on the proteins. Their action is essentially connected with the function of breaking up dead organic nitrogenous material, so that it is finally converted into ammonia. Hence, the function of these organisms is essentially proteolytic.

In the laboratory the two classes of organisms are readily distinguished by their action on litmus milk. Fat-free milk is coloured lilac by the addition of litmus, and is then sterilized. Inoculated with the *Streptococcus lacticus*, the milk curdles, and the fluid becomes red, as a result of the action of the acid on the litmus. Inoculated with the *Bacillus subtilis*, the milk curdles, but there is no alteration in the colour of the litmus.

A day or two after the curdling of the specimen inoculated with the *Bacillus subtilis*, three layers may be observed. The uppermost layer is blue, the intermediate layer is yellowish-brown and somewhat translucent, the lowest layer consists of the precipitated protein not yet taken into solution. At a still later stage the whole of the solid matter is digested, the blue colour is destroyed, and a viscid brown fluid occupies the tube.

There is one striking feature which is characteristic of the lactic organisms and which is in striking contrast to the properties of the other group. All the lactic organisms are extremely delicate. They are extraordinarily sensitive to heat, being destroyed at very low temperatures. The *Streptococcus lacticus* growing in pure culture, in its most favourable medium, will die out in the course of about a fortnight, so that the medium becomes as sterile as it was before it was inoculated. The *Bacillus acidi lactici* behaves in precisely the same manner. The *Bacillus Bulgaricus* lives for a little longer, but in about a month the medium inoculated with this organism will become sterile.

I have introduced these considerations in regard to the biology and chemistry of milk at the very outset of my paper, for they are of fundamental importance. The problems involved in these biochemical considerations are the problems of infancy.

I pass now to certain general considerations in regard to the incidence of epidemic diarrhœa in this country. It is the most fatal disease of infants. The great progress in sanitation has had no effect in staying the disease. Newman,[1] indeed, has shown

[1] "Infant Mortality" (London, 1906), pp. 55, 56.

that the disease is steadily increasing as a factor in the causation of death among infants under one year of age :

"Diarrhœa, which formerly caused the death of 10 per cent. of dead infants, has increased in half a century to 15 per cent. ; respiratory diseases have risen from 16 to 18 per cent. ; and prematurity from 17 to 29 per cent. . . . Other children's diseases are vanishing, or have vanished. There has been a vast improvement in the general environment surrounding their lives, but the problem of infantile mortality still remains, because of the *increase* in these diseases—prematurity, pneumonia, and diarrhœa."

The increase in the proportion of deaths from respiratory diseases is probably closely connected with the increase in diarrhœa. Healthy infants are not very frequently attacked by serious disease of the lung as a primary affection. In a certain number of quite young infants a subacute bronchitis may be observed. It is very chronic in character, and it is generally stated to have been present at birth or soon afterwards. This is the common type of bronchitis in infants who are born the victims of congenital syphilis.

In conditions of enteritis, pneumonia is extremely likely to develop as a complication. It occasionally occurs in the acute disease, but it is commonly seen accompanying the more chronic conditions. It is a frequent accompaniment or sequela of atrophic enteritis, and many infants suffering from this disease contract pneumonia as a terminal affection.

The disease is most prevalent and most fatal during the third quarter of the year. The higher the tem-

perature of the late summer, the greater the prevalence of the disease, especially if this high temperature be associated with but little rain. In other words, meteorological conditions involving a high temperature with much dust are those which promote the conditions which accompany the greatest incidence of the disease.

The classical researches of Ballard,[1] the more recent researches of Newsholme,[2] and the observations made by many Medical Officers of Health, all establish clearly that the essential factors are high temperature and dust, with special reference to the part they play in the contamination of milk. Three of Newsholme's conclusions are of particular importance:

1. Epidemic diarrhœa is chiefly a disease of urban life.

2. Epidemic diarrhœa as a fatal disease is a disease of the artisan and still more of the lower labouring classes to a preponderant extent. This is probably largely a question of social status *per se*—that is, it is due to neglect of infants, uncleanly storage of food, industrial occupation of mothers, etc.

3. The fundamental condition favouring epidemic diarrhœa is an unclean soil, the particulate poison from which infests the air and is swallowed, most commonly with food, especially milk.

It is essential to the comprehension of the disease that the common conception that it belongs to the group of specific infectious diseases should be abandoned. Epidemic diarrhœa is in no sense of the word

[1] Supplement to the Report of the Medical Officer of the Local Government Board, 1887.

[2] *Public Health*, 1899-1900.

an infectious disease, and it cannot be conveyed by contagion.

The work of the Infants Hospital is confined exclusively to infants under twelve months of age. All the infants when admitted are seriously ill, most of them desperately so. At the times that epidemic diarrhœa is prevalent very numerous cases are admitted, mostly of an extremely severe type. No infant has ever contracted the disease in the hospital. The only infants suffering from it are those suffering from the disease at the time of admission. No attempt at isolation is made. The infants lie side by side in their cots—the case of severe atrophy next the case of epidemic diarrhœa—and they are all tended by the same nurses, who minister to all their requirements.

Precisely the same thing is seen outside the hospital. At a time that the disease is sweeping through a town, destroying some hundreds of infants per thousand in the course of a month or two, there are babies living in the most insanitary conditions who are immune—they are the breast-fed babies. There is no need to labour this point, for numerous Medical Officers of Health have drawn attention to the same fact.

Between the circumstances of the poor Irish breast-fed baby living in a London slum and those of the infant warded in the Infants Hospital there is a wide contrast. There is also a remarkable correspondence—both are fed on a pure *raw* milk. The infants at the hospital are protected by something much more powerful than isolation, for it is a practical impossibility for the violent fatal disease known as epidemic diarrhœa to occur in an infant fed on fresh milk. It is essential for the development of the disease

that the characteristic properties of the natural food of the infant should have been destroyed by heat, by preservatives, or by some other means.

I conclude this section by quoting the propositions formulated by Ballard in 1887, "as a working hypothesis that would best accord with the totality of the evidence."

"That the essential cause of diarrhœa resides ordinarily in the superficial layers of the earth, where it is intimately associated with the life-processes of some micro-organism not yet detected, captured, or isolated.

"That the vital manifestations of such organism are dependent, among other things, perhaps principally upon conditions of season and on the presence of dead organic matter which is its pabulum.

"That on occasion such micro-organism is capable of getting abroad from its primary *habitat*, the earth, and having become air-borne, obtains opportunity for fastening on non-living organic material, and of using such organic material both as nidus and as pabulum in undergoing various phases of its life-history.

"That in food inside of, as well as outside of, the human body, such micro-organism finds, especially at certain seasons, nidus and pabulum convenient for its development, multiplication, or evolution.

"That from food, as also from the contained organic matter of particular soils, such micro-organism can manufacture by the chemical changes wrought therein through certain of its life-processes, a substance which is a *virulent chemical poison;* and that this chemical substance is, in the human body, the material cause of epidemic diarrhœa."[1]

[1] Supplement to the Report of the Medical Officer of the Local Government Board, 1887.

## II

## On the Relationship of the Disease to the Diarrhœas of Infancy

One of the most unfortunate facts in regard to the disease is that it should be named officially by a symptom. The intensity of the diarrhœa affords no criterion of the severity of the disease. On the contrary, the worst cases, as a rule, are those in which diarrhœa is not a prominent symptom or is entirely absent. Emmett Holt, in his "Diseases of Infancy and Childhood," particularly refers to the cases in which constipation occurs, and he adds that when one meets such a case, he can appreciate the fact that in acute intestinal intoxication diarrhœa is a conservative process of the greatest possible value. A point of great interest in this connection is the statement of Ballard in 1887 that, in his opinion, the disease could run its course from first to last, and even to death, without any diarrhœa at all. In the experiments to be described, diarrhœa was an extremely variable factor.

In infancy, disorder of the alimentary tract in the shape of diarrhœa occurs in numerous conditions. In broncho-pneumonia it is extremely common. In congenital syphilis a peculiarly intractable diarrhœa, only yielding to systematic mercurial treatment, is not uncommon, while in the more trivial affections diarrhœa is of extremely frequent occurrence.

At the Infants Hospital I occasionally order the milk for a particular infant to be heated to 150° F. (65·6° C.), and further prescribe that the greater part of the sugar in the milk shall be cane-sugar instead of milk-sugar. The infant for whom such a mixture is ordered is suffering from excessive lactic fermentation, which is giving rise to acid diarrhœa. The milk is heated so as to destroy the lactic organisms which it contains, while the lactose is much diminished, in order to deprive the lactic organisms in the intestine of the material from which they produce the acid. Gradually, as the symptoms subside, the infant is placed upon raw milk with the normal proportion of lactose.

In all such cases the prognosis is as good as it is bad in cases of intestinal toxæmia. Nevertheless, alimentary disorders of the character referred to are extremely serious when allowed to continue unchecked for a considerable period. The exhaustion caused by the constant diarrhœa and the consequent deprivation of nourishment necessarily entails serious consequences.

But in this paper I am not discussing the alimentary disorders of infancy which occur all the year round. I am dealing with a disease which kills infants in the hot weather in a manner which can only be compared with the plague in the Middle Ages. It kills so quickly, and it kills so many.

I lay emphasis upon this, because of the chaos of diagnosis and terminology necessarily involved in a nomenclature based upon symptoms—and of all symptoms that symptom which is the most protean in its forms and causes.

I have always refused to accept the term "Epidemic Diarrhœa." For a time I struggled with one of the official alternatives, "Zymotic Enteritis," but I could not continue to use a term so acadabraic. I have therefore been compelled to abandon the official nomenclature and have adopted the term "Acute Intestinal Toxæmia."

## III

## On the Experimental Production of the Disease in Animals

The experimental investigation to be described was preceded by certain preliminary inquiries, with a view to determine the precise procedure to be followed in the experiments.

It was decided to select kittens for the experiments, as they were the suckling animals that could most readily be obtained, and because the whole of the cat tribe is extremely powerful in its resistance to intestinal affections.

Inasmuch as the disease is practically limited to infants, it was necessary to select kittens at a suckling age. These animals rapidly mature, and a kitten able to thrive upon cats' meat is generally immune. Kittens were therefore selected at about two months of age and weighing about one pound.

Some preliminary experiments were carried out on monkeys. They were quite immune. Monkeys fed on sterilized milk inoculated with the *Bacillus subtilis* thrived upon the food. They were, of course, long past the suckling age. Had I been able to obtain monkeys during "infancy," I have little doubt that they would have rapidly succumbed.

All the kittens experimented upon were first fed on

fresh unheated milk, and only those in good condition in every way were selected for experiment.

With the exception of the experiment with condensed milk, the milk used was taken directly from the milk laboratory of the Infants Hospital, and was a sample of the bulk milk used for the infants. In a few instances milk is ordered to be peptonized or heated to meet special indications, but over 90 per cent. of the infants receive their milk in its raw condition. This, therefore, constitutes an important and extensive control.

Each experiment was conducted with four kittens. They were fed four times in the twenty-four hours—at 8 a.m., noon, 4 p.m., and 8 p.m. At each meal a new bottle was used, so that the milk was protected from any possible contamination. Strict precautions were adopted to prevent milk lying about in the cages, all débris being washed away with water, in which washing soda was dissolved. All utensils used in the feeding were boiled immediately before feeding the animals, and cleansed immediately afterwards with a solution of washing soda. Fifteen minutes were allowed for the animals to take the milk, and the saucers were then removed.

In the first experiment milk taken directly from the milk laboratory was placed in sterilized bottles and sealed with sterilized cotton-wool. It was raised to 200° F. (93·3° C.), and then incubated for twenty-four hours at 85° F. (29·4° C.). The temperature of 200° F. was adopted because it represents, approximately, the temperature attained by the mother when she "boils" or "scalds" the milk. The milk in these circumstances seldom reaches 212° F.

All the kittens fed on this milk died from the disease, but, in comparison with the others, the experiment was only a partial success. There was evidently some disturbing factor, and this factor was the *Bacillus enteritidis sporogenes*. It may at once be said that this organism could not possibly develop in either raw milk or in boiled milk in the home, for it is a strict anaerobe. The growth of this organism only occurred on three occasions (July 14, July 29, and August 1). The organism is destroyed by a temperature of 212° F. (100° C.) for one minute or at 180° F. (82° C.) for thirty minutes; and since the temperature of the milk was gradually increasing from 180° to 200° F. over a period of some fifteen minutes, it is clear that on all the other occasions either the organism was not present in the milk, or the temperature on these occasions was sufficient to destroy it, or the conditions were not anaerobic. How did it happen that the conditions were anaerobic? This arose from the gradual driving off of the air during the heating, the settling of a layer of fat on the top of the milk so as to act as a seal, and the stationary condition of the bottles during the incubation period. To destroy the anaerobic condition it would have been only necessary to vigorously shake the bottles after the boiling. I purposely refrained from having that done after detecting the abnormality on July 14, as I foresaw that the comparative failure of the experiment might provide valuable information, and the experiment, as designed at the outset, was carried out to the end.

The result of this development of an acid-producing organism would naturally be to completely upset for the time the object of the experiment. Not only

would the kittens be receiving a culture of an organism which does not belong to the putrefactive group, but they would also receive a fresh supply of acid-producing organisms, which would enable them the more effectively to combat the putrefactive bacteria. The growth of this organism in milk produces a quite characteristic appearance, so that the observer can at once suspect the organism responsible.

Experiment X. was a repetition of the first experiment, with the exception that the milk was raised to 212° F. (100° C.), and maintained at that temperature for three minutes. The rapid appearance of the disease in this experiment is in marked contrast to the slow onset in the first experiment.

In all experiments subsequent to the first, where "boiling" was resorted to, the milk was raised to 212° F., and maintained at this temperature for three minutes. One other point is of some interest: As I have pointed out, the anaerobic conditions are more or less fulfilled in the case of boiled or sterilized milk kept stationary. This means that the cultural conditions were not those favouring the maximum development of the putrefactive organisms in the milk, for all these organisms grow most freely when oxygen is freely available.

### Experiment I.

Four kittens fed on milk raised to 200° F. (93·3° C.), and then incubated for twenty-four hours at a temperature of 85° F. (29·4° C.). Experiment begun June 23. Experiment ended (death of last surviving kitten) August 7. Kittens numbered 1 to 4.

*Kitten* 1.—For the first two days the intestinal

dejections were normal. On June 26 they became firm and dark brown in colour. On June 26 the dejections during the night were rather loose and yellow in colour. One dejection was passed during the day, and was brown in colour and paste-like in consistence. On the night of June 29 moderate diarrhœa occurred. On the 30th the diarrhœa increased, the dejections being very liquid, large in amount, and frequent.

On July 1 the condition improved; the dejections were less frequent, and were of firmer consistence. In twelve hours diarrhœa again occurred, and continued till July 3, when the dejections became very stiff and greyish in colour. On July 5 diarrhœa again occurred, but on July 6 constipation set in. Nothing was passed on July 7, and the kitten looked ill, and took very little milk. On July 8 there was no action; the kitten was taking very little milk, looked very ill, and the trembling was marked. This condition continued until July 11, when the kitten became collapsed, and died during the early hours of July 12.

The kitten weighed 16 ounces at the beginning of the experiment, and 14 ounces at the end—a loss of 12·5 per cent.

*Kitten* 2.—On June 23 and 24 the motions were normal, but the kitten objected to the boiled milk, and for these two days took very little milk. On June 25 it took the milk well, and no further difficulty was experienced with regard to this.

The dejections continued to be normal until June 28, when slight diarrhœa occurred. This continued until June 30, when the dejections became greenish in colour, and were rather pasty in consistence. On

July 1 there was slight diarrhœa. On July 2 this ceased. On July 3 diarrhœa again appeared, and now continued, with occasionally temporary improvements, until July 18, when the kitten was noticed to be looking ill, and was rather weak. This condition continued until the 22nd, when the kitten looked much better, although the diarrhœa still continued. On July 25 the diarrhœa ceased ; the kitten again became ill, and took very little milk. On July 26 the kitten became very ill and weak, and diarrhœa re-appeared ; the dejections were very watery, yellowish in colour, and some of them contained traces of blood. On the 27th the kitten was comatose, and died at 2 p.m.

The kitten weighed 13 ounces at the beginning of the experiment, and 10½ ounces at the end—a loss of 19·25 per cent.

*Kitten* 3.—For the first two days the kitten took very little milk. The dejections were normal. It then took well. On June 26 the dejections were dark brown and firm. On June 27 the dejections were yellow, rather loose, but there was no diarrhœa. On the 28th there was slight diarrhœa. On the 29th the diarrhœa had ceased and the dejections became dark and pasty. On the 30th there was diarrhœa. This continued until July 3, when the dejections became very stiff and pasty, although fairly frequent. The condition continued until July 8, when the dejections became loose and watery. This was more marked on the following day. The diarrhœa continued until July 12, when the dejections again became pasty in consistence. This alternation of diarrhœa with pasty dejections continued until August 5, when diarrhœa

was again established, and continued till the kitten died on August 7. On August 5 the kitten looked ill and was rather weak. On August 6 the animal was very weak and ill, the eyes were dull, and there was trembling of the whole body. It died in the night.

The weight was 14 ounces at the beginning of the experiment, and 11½ ounces at the end—a loss of 17·8 per cent.

*Kitten* 4.—During the first day the kitten took very little milk. After this it took well. The dejections were normal for the first three days. On June 26 they were firm and dark brown in colour, becoming loose and yellow in the late part of the day. On the 29th there was diarrhœa. On the 30th the dejections became pasty and sticky and greyish in colour. This condition continued until July 3, when there was a sharp attack of diarrhœa. This ceased on July 4, but there was diarrhœa again on July 5 and 6. On July 7 this became more marked, the dejections being very watery and frequent. From July 8 to July 16 the dejections were not frequent, but the intestines acted at least twice in the twenty-four hours, and the material was greyish in colour, stiff, and paste-like. During the day of July 17, and during the whole of the 18th, there was complete constipation, no dejection being passed. On July 18 the kitten was very weak, the eyes were dull, and on July 19 the motions were very stiff, pasty, and greyish. The kitten was very weak and apathetic. On July 20 the dejections were still paste-like and very firm. The kitten was very ill, and at times almost unconscious, but it still continued to take fair amounts of milk. On July 21 there was no action. The

kitten was taking very little milk. It was very weak, and there was marked trembling of the whole body. It died during the night.

The kitten weighed 20 ounces at the beginning of the experiment, and 14 ounces at the end—a loss of 30 per cent.

EXPERIMENT I.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 1 | June 23 | July 12 | 19 days | 12·5 |
| Kitten 2 | June 23 | July 27 | 34 days | 19·25 |
| Kitten 3 | June 23 | Aug. 7 | 45 days | 17·8 |
| Kitten 4 | June 23 | July 22 | 29 days | 30·0 |

Average duration of experiment, 32 days.
Average loss in weight, 19·5 per cent.

Experiment II. was carried out by pure culture.

Sterilized milk (sterilized by heating at 212° F. [100° C.] for one hour on four successive days) was inoculated with a pure culture of the *Bacillus subtilis* and incubated for twenty-four hours.

## EXPERIMENT II.

Four kittens fed on sterilized milk inoculated with the *Bacillus subtilis* and incubated at a temperature of 85 F. (29·4 C.). Experiment begun June 25, 1910; ended July 5 (death of last surviving kitten). Kittens numbered 5 to 8.

*Kitten* 5.—The kitten took the milk well from the start. The first day the dejections were normal. On the following day they became very firm and dark brown in colour. No change occurred till June 29, when diarrhœa was established, the dejections being loose and pale yellow. On the 30th there was slight diarrhœa, and traces of blood were observed. The

kitten was very weak, there was marked trembling of the body, the animal was very apathetic, almost unconscious, and the eyes were dull. It took milk fairly well up till late on June 30. It died during the night.

It weighed 12 ounces at the beginning of the experiment, and $9\frac{1}{2}$ ounces at the end—a loss of 20·8 per cent.

*Kitten* 6.—The kitten took the milk well from the start. In the first twenty-four hours the dejections were normal. On June 26 the dejections became dark brown and firm, and continued so till late on the 27th, when they became looser, but remained the same colour. On June 28 diarrhœa was established, the dejections being light yellow in colour. On the 29th diarrhœa was still present, the dejections being very loose. On the 30th the diarrhœa continued, traces of blood being observed. On July 1 the diarrhœa still existed, but was milder, and no blood was observed. On July 2, the diarrhœa was again established. On the afternoon of July 3 the diarrhœa ceased and the dejections were semi-solid. On the morning of July 4 there was no diarrhœa. The dejections were dark yellow or brown, and of paste-like consistence. In the afternoon there was a renewal of the diarrhœa. The kitten was now very weak and ill, and nearly unconscious. It died during the night, having taken very little milk in the previous twenty-four hours.

The kitten weighed 15 ounces at the beginning of the experiment, and 12 ounces at the end—a loss of 20 per cent.

*Kitten* 7.—The kitten took the milk well. For the first twenty-four hours the dejections were normal. They then became dark brown and firm. There was no

change until the night of June 28, when moderate diarrhœa was established, the dejections being yellowish-white in colour. The frequent dejections continued, but on June 30 they were paste-like and contained traces of blood. The kitten was very weak, was trembling, and was nearly unconscious. It died during the night.

The weight of the kitten at the beginning of the experiment was 14 ounces, and $11\frac{1}{4}$ ounces at the end —a loss of 19·6 per cent.

*Kitten* 8.—The kitten took the milk well, and for the first twelve hours the dejections were normal. They then became dark brown and rather loose. On June 27 the dejections were dark brown and firm. On the 28th marked diarrhœa occurred, the dejections being yellowish-white. This condition continued until July 2, when the dejections became a little firmer. On July 3 the diarrhœa was very marked, the dejections being dark in colour. The kitten was very weak and trembling, and very apathetic. During the night the dejections were streaked with blood. The kitten died on July 4 at 9 a.m.

The kitten weighed 14 ounces at the beginning of the experiment, and 11 ounces at the end—a loss of 21·4 per cent.

Experiment II.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 5 ... | June 25 ... | July 1 ... | 7 days ... | 20·8 |
| Kitten 6 ... | June 25 ... | July 5 ... | 10 days ... | 20·0 |
| Kitten 7 ... | June 25 ... | July 1 ... | 7 days ... | 19·6 |
| Kitten 8 ... | June 25 ... | July 4 ... | 9 days ... | 21·4 |

Average duration of experiment, 8·25 days.
Average loss in weight, 20·4 per cent.

The third experiment was the beginning of a series in which the milk mixtures closely resembled the kind of food commonly received by the infant in the home. A well-known brand of condensed milk was taken, and it was diluted with water in accordance with the instructions given on the tin for feeding an infant three months old. The mixture was then placed in bottles, sealed with cotton-wool, and was raised to a temperature of 212° F. (100° C.) for three minutes. (This precaution was adopted in order to avoid the introduction of lactic organisms—a possibility that could not be ignored in an institution where large quantities of raw milk are constantly being handled.) The mixture was then incubated for twenty-four hours at 85° F. (29·4° C.). Incidentally, I may remark, that a tin of condensed milk affords an extremely convenient means of obtaining the spore-forming putrefactive bacteria in almost pure culture. The lactic organisms are entirely destroyed, and if a sterile platinum loop be dipped into the freshly opened tin of condensed milk, and agar plates be inoculated from the loop (after suitable dilution), it will generally be found that the growth consists of two, three, or four varieties of these organisms, and of no others.

### Experiment III.

Four kittens, fed on diluted condensed milk heated to 212° F. (100° C.) and incubated at a temperature of 85° F. (29·4° C.) for twenty-four hours. Experiment begun July 23. Experiment ended (death of last surviving kitten) August 5. Kittens numbered 9 to 12.

*Kitten* 9.—The kitten took the milk fairly well on

the first day. The dejections were normal. In the night they were pasty in consistence and yellow in colour. On July 25 they were very stiff and paste-like, dark brown and greenish in colour. On July 26 there was constipation, no dejection being passed. The kitten was weak and ill, and only took about half the quantity of milk it had previously taken. On July 27 the dejections were very firm and dark brown. The kitten was ill, weak, and there was trembling of the whole body. The kitten then became comatose, and died at 9 a.m. on July 28. It weighed 13 ounces at the beginning of the experiment, and 11 ounces at the end—a loss of 15·3 per cent.

*Kitten* 10.—The dejections were normal at the beginning of the experiment. On July 24 they became pasty and greyish in colour. On July 25 they were still pasty, but dark brown in colour. This condition obtained till July 28, when there was complete constipation, no dejection being passed. The kitten looked ill and weak, and was only taking small quantities of the milk. On July 29 there was no dejection. The animal was very weak and ill, the eyes being very dull. On July 30 the intestines acted, the dejection being pasty in consistence and blackish in colour. The kitten was very collapsed, and there was marked trembling. During the last twenty-four hours it was comatose. It died on July 31 at 7 p.m.

The kitten weighed 17 ounces at the beginning of the experiment, and 12 ounces at the end—a loss of 29·4 per cent.

*Kitten* 11.—The dejections were normal at the beginning of the experiment. On July 24 they became pasty and greyish in colour. This condition

obtained till July 27, when there was no intestinal action. On July 28 the intestines acted; the dejections were very firm and dark brown. On July 29 diarrhœa occurred, the dejections being yellowish-white and very liquid. This condition continued for some days. On August 2 the kitten was ill and weak, the eyes being dull. On August 3 there was no intestinal action. The animal was taking very little milk and was very ill, trembling of the whole body being marked. On August 4 very little food was taken, and there was no intestinal action. The animal became comatose. It remained in this condition until it died at 4 p.m. on August 5.

The kitten weighed 18 ounces at the beginning of the experiment, and 14 ounces at the end—a loss of 22·2 per cent.

*Kitten* 12.—The dejections were normal at the beginning of the experiment, but became paste-like and of greyish colour on July 24. On July 26 the dejections were dark green. On July 28 it was noted that there had been no action during the night, and the kitten looked ill and was rather weak. During the day the intestines acted, the dejections being very firm and dark greenish-brown. The kitten looked rather better and brighter. On July 29 it looked ill and weak in the morning, but improved during the day. On July 30 there was no intestinal action, and the animal looked poorly. On July 31 the dejections were firm and dark greenish-brown. This condition obtained until August 2, when moderate diarrhœa set in, the dejections being greyish in colour. On August 3 the kitten was again ill and weak, the moderate diarrhœa continuing. On August 4 the

kitten was ill and trembling, the diarrhœa was marked, though not severe. The kitten died during the night.

The kitten weighed 18 ounces at the beginning of the experiment, and 13 ounces at the end—a loss of 38·4 per cent.

EXPERIMENT III.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 9 ... | July 23 ... | July 28 ... | 5 days ... | 15·3 |
| Kitten 10 ... | July 23 ... | July 31 ... | 8 days ... | 29·4 |
| Kitten 11 ... | July 23 ... | Aug. 5 ... | 13 days ... | 22·2 |
| Kitten 12 ... | July 23 ... | Aug. 5 ... | 13 days ... | 38·4 |

Average duration of experiment, 9·7 days.
Average loss in weight, 26·3 per cent.

The next experiment was carried out with a mixture representing the composition of a milk-mixture obtained by diluting milk with an equal quantity of water, and then adding cream and cane-sugar, to restore the fat and sugar content to the normal standard. The composition of the modified milk used in this and in subsequent experiments was as follows :

| | Per Cent. |
|---|---|
| Fat ... ... ... ... | 3·50 |
| Milk-sugar ... ... ... | 2·50 |
| Cane-sugar ... ... ... | 4·00 |
| Proteins ... ... ... | 1·75 |

The mixture was raised to 212° F. (100° C.), and maintained at this temperature for three minutes. It was then incubated for twenty-four hours at 85° F. (29·4° C.).

EXPERIMENT IV.

Four kittens fed on modified cow's milk maintained at a temperature of 212° F. (100° C.) for three minutes,

and then incubated at 85° F. (29·4° C.) for twenty-four hours. Kittens numbered 13 to 16. Experiment begun July 25. Experiment ended (death of last surviving kitten) August 23.

*Kitten* 13.—On July 25 the dejections were normal. On the 26th they became pasty and greyish. No diarrhœa. On the 27th there was constipation, the dejections being very firm and dark. The kitten looked ill and was rather weak. It had a discharge from the eyes, and was taking very little milk. From this time the kitten remained ill and weak, taking very little food, the dejections being very firm and greyish in colour. On August 2 slight trembling was noticed. On August 3 the kitten was collapsed, and the trembling was marked. It then became comatose and died at 2 p.m.

The kitten weighed 20 ounces at the beginning of the experiment, and 14 ounces at the end—a loss of 30 per cent.

*Kitten* 14.—The dejections were normal on the first day. On July 26 they became pasty and greyish. On July 27 they were pasty and dark brown. This condition obtained until July 30, when there was marked constipation. There was no intestinal dejection on July 30 or July 31, but on August 1 the intestines acted, the dejections being very firm and dark brown. On August 2 there was no change. On August 3 the animal was ill and weak, and there was slight trembling. On August 4 there was no intestinal action. The kitten was very weak, could not stand, the eyes were dull, and the body was trembling. Practically no food was taken during this day. On August 5 there was diarrhœa, the dejections being

very loose and yellowish in colour. Later in the day the animal became comatose. It died during the night.

The weight of the animal was 18 ounces at the beginning of the experiment, and 12½ ounces at the end—a loss of 30·5 per cent.

*Kitten* 15.—The dejections were normal at the beginning of the experiment. They became pasty and greyish on July 26. On the 27th they were dark brown and pasty. On the 28th and 29th there was no intestinal action. On the 30th the dejections were dark brown and firm. This condition obtained until August 4, when there was no action. The kitten, however, looked well. On August 5 the dejections were dark brown and firm. On August 6 there was no action. On August 7 the dejections were yellowish in colour, but very firm. On August 8, 9, and 10 there was no action. On August 11 the dejections were brown and firm. On August 12 the dejections were yellowish, but still firm. The kitten looked weak and ill. On August 13 the dejections remained the same, but the animal was much brighter. On August 14 there was no intestinal action, and the kitten was weak and ill. On August 15 the dejections were yellow and firm; the animal was very weak, the eyes were dull, and there was marked apathy. On August 16 the animal took very little milk, was very ill and weak, and there was slight trembling. No dejection. The kitten died at 9.30 a.m. on August 17.

The weight of the kitten was 18 ounces at the beginning of the experiment, and 12 ounces at the end —a loss of 33·3 per cent.

*Kitten* 16.—The dejections were normal at the beginning of the experiment. On the 26th and 27th

they were yellow and rather pasty. On July 28 there was slight diarrhœa, the colour being dark brown. On the 29th the dejections were firm and dark brown in colour. There was no action on July 30 or 31. On August 1 and 2 the dejections were firm and blackish-brown in colour. On the 3rd and 4th there was again no dejection. From August 5 to August 13 the dejections were of rather pasty consistence and yellow in colour, there being one or two in the course of twenty-four hours. During the night of August 14 there was diarrhœa, the dejections being watery and yellow. This ceased in the day, and the dejections resumed their usual character. This condition obtained until August 20, when the dejections became greyish in colour, of firm consistence, and sticky. On August 21 the animal looked rather ill and weak; the eyes were dull. On August 22 the animal was very ill and apathetic. At 8 p.m. it was collapsed and comatose. It died during the night.

The weight of the kitten was 19 ounces at the beginning of the experiment, and $12\frac{1}{2}$ ounces at the end—a loss of 31·5 per cent.

Experiment IV.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 13 | July 25 | Aug. 2 | 8 days | 30 |
| Kitten 14 | July 25 | Aug. 6 | 12 days | 30·5 |
| Kitten 15 | July 25 | Aug. 17 | 23 days | 33·3 |
| Kitten 16 | July 25 | Aug. 23 | 29 days | 31·5 |

Average duration of experiment, 18 days.
Average loss in weight, 31·3 per cent.

The fifth experiment was carried out with modified milk sterilized and then inoculated with a pure culture

of the *Bacillus mesentericus vulgatus*. It was then incubated for twenty-four hours at a temperature of 85° F. (29·4° C.).

### Experiment V.

Four kittens fed on sterilized modified milk inoculated with the *Bacillus mesentericus vulgatus* and inoculated for twenty-four hours at 85° F.

Kittens numbered 17 to 20. Experiment begun August 15. Experiment ended (death of last surviving kitten) August 25.

*Kitten* 17.—The dejections were normal at the beginning of the experiment. On August 16 there was moderate diarrhœa, the dejections being rather frequent, watery, and yellow in colour. This continued during the first part of the 17th, but was replaced by constipation in the later twelve hours. This constipation continued on the 18th. On this morning the kitten looked ill and rather weak. During the day it became worse. The eyes were dull, and the animal was markedly apathetic. It was now taking very little milk. On the 19th the dejections were firm and paste-like, and dark brown in colour. The animal was very ill and comatose. During the day it became quite collapsed, lying in its cage apparently dead. It was breathing very slowly. It remained in this condition until it died at 3 p.m. on August 20.

The kitten weighed 13 ounces at the beginning of the experiment, and 11 ounces at the end—a loss of 15·3 per cent.

*Kitten* 18.—The dejections were normal at the beginning of the experiment. On August 16 a sharp attack of diarrhœa occurred, the dejections being very

watery, frequent, and pale yellow in colour. This continued until the afternoon of the 17th, when constipation set in, and there was no dejection till the morning of the 19th. The dejections then were firm and dark in colour. From this time to August 22 there was constipation. The kitten looked weak and ill, and the eyes were dull. It took very little milk on this and the succeeding days. On the 23rd there was one firm dark dejection. The animal was very ill, and there was slight tremor of the whole body. On the 24th the kitten was very apathetic, there was marked tremor of the whole body. During the day the tremor gradually ceased, and the animal became comatose. There was one dejection on this day, which was very firm and dark brown in colour. The kitten died during the night.

At the beginning of the experiment it weighed 15 ounces, at the end 11 ounces—a loss of 26·6 per cent.

*Kitten* 19.—The dejections were normal at the beginning of the experiment. On August 16 and 17 they were light brown in colour and pasty. On August 18, 19, and 20 the animal was constipated, and no dejections were passed. On the 20th the kitten looked ill and weak, and took but little milk. On the 21st the dejections were firm and dark brown. The animal was very ill and apathetic. The eyes were dull. Later in the day it became collapsed, and there was marked tremor of the whole body. The animal then became comatose. The last dejection on the 21st was semi-solid and dark brown in colour. The kitten died in the early morning of the 22nd.

At the beginning of the experiment it weighed 14 ounces, at the end 11 ounces—a loss of 21·4 per cent.

*Kitten* 20.—The dejections were normal at the beginning of the experiment. On the 16th they became pasty and yellowish in colour. On the 17th and 18th no dejection was passed. On the 19th they were firm, pasty, and brown in colour. The same condition obtained on the 20th. On the 21st there was no dejection. The animal was weak and ill. On the 22nd the dejections were very firm and dark brown. The kitten was ill, apathetic, and the eyes were dull. On August 23rd there was no dejection. The kitten was taking very little milk. It was very weak and ill. On the 24th, in the early part of the day, it looked much better, being bright and quite conscious. Later in the day it relapsed into the condition of weakness and apathy. There was no dejection. On the 24th, in the early morning, there was one dejection which was very firm and yellow in colour. The kitten was comatose, and died at 10 a.m.

The weight at the beginning of the experiment was $12\frac{1}{2}$ ounces, at the end 10 ounces—a loss of 20 per cent.

Experiment V.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 17 | Aug. 15 | Aug. 20 | 5 days | 15·3 |
| Kitten 18 | Aug. 15 | Aug. 25 | 10 days | 26·6 |
| Kitten 19 | Aug. 15 | Aug. 22 | 7 days | 21·4 |
| Kitten 20 | Aug. 15 | Aug. 24 | 9 days | 20·0 |

Average duration of experiment, 7·7 days.
Average loss in weight, 20·8 per cent.

The next experiment was with sterilized modified milk inoculated with the *Bacillus mesentericus* ("No. 7" Infants Hospital Research Laboratory).

### Experiment VI.

Four kittens fed on sterilized modified milk inoculated with the *Bacillus mesentericus* ("No 7") and incubated for twenty-four hours at 85° F. (29·4° C.). Kittens numbered 21 to 24. Experiment begun August 15. Experiment ended (death of last surviving kitten) August 30.

*Kitten* 21.—The dejections were normal on the first day of the experiment, and they remained so on August 16. On August 17, 18, and 19, the dejections were infrequent, there being none during the night and only one during the day. There was no diarrhœa, the dejections being paste-like and yellow in colour. On August 20 the kitten was weak and ill, and these signs increased during the day. The dejections were still of the character described. On August 21 the animal was comatose. There was one intestinal dejection which was firm in consistence and dark brown in colour. The kitten died at 4 p.m.

The weight was 17 ounces at the beginning of the experiment, and 12 ounces at the end—a loss of 29·4 per cent.

*Kitten* 22.—On August 15 the dejections were normal. On August 16 there was an attack of diarrhœa, the actions being very watery and frequent. This ceased during the day, and on August 17 the dejections were very firm in consistence and dark brown. On August 18 the dejections were firm and yellow. There was no change on the 19th. On August 20 there was no action. There was none on August 21, and the kitten was weak and looked ill. On the 22nd the kitten was very weak and ill and apathetic. The dejections were firm and dark. On

August 23 there was no dejection. The kitten was very ill, the whole body was trembling, and the eyes were dull. The condition remained the same on the 24th. The kitten was now taking very little milk, and there was no intestinal action. From this time the kitten remained very ill, and taking very little food. On August 27 it became comatose, lying in its cage quite motionless. It died in the early hours of August 28. The animal had been in a moribund condition for the previous four days.

The kitten weighed 19 ounces at the beginning of the experiment, and 13 ounces at the end—a loss of 31·5 per cent.

*Kitten* 23.—The dejections remained normal for the first two days. On August 17, 18, and 19 there was no dejection. On August 20 and 21 the dejections were yellowish and pasty. On August 22 the dejections were dark brown and of firm consistence. The kitten appeared weak and ill. The condition remained about the same on the 23rd, the dejections being of the same character as on the previous day. On August 24 the animal was very weak and ill, the eyes very dull ; but during the day its condition improved, the animal becoming much brighter and more active. There was no dejection. On August 23 the weakness had returned, and the kitten looked ill ; the eyes were again very dull. The dejections were firm in consistence, and almost black in colour. On the 26th there was no action, and the animal was very ill. On the 27th the illness increased, and the animal was barely conscious. On August 28th it was very collapsed. The eyes were dull and there was tremor of the whole body. It died at 3 p.m.

The kitten weighed 18 ounces at the beginning of the experiment, and 11½ ounces at the end—a loss of 36·1 per cent.

*Kitten* 24.—On August 15 the dejections were normal. On the 16th and 17th there was moderate diarrhœa, the dejections being yellow in colour. This condition continued till August 20, when the dejections became firm and greyish in colour. On the 21st there was no change. On the 22nd the dejections were pasty and yellow. On August 24 there was no action. On August 25 the dejections were greyish in colour and firm. The kitten looked rather ill. On the 26th there was no change. On the 27th the kitten was weak and looked very ill. There was no dejection. On August 28 the illness was marked ; the dejections were firm and yellow. On August 29 there was no change, except that the weakness was more pronounced. On August 30 the dejections were firm and yellow. The animal was very ill, and there was marked tremor of the whole body. Later in the day this ceased, and the animal became comatose. It died at 7 p.m.

The kitten weighed 19½ ounces at the beginning of the experiment, and 12½ ounces at the end—a loss of 35·8 per cent.

Experiment VI.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 21 | Aug. 15 | Aug. 21 | 6 days | 29·4 |
| Kitten 22 | Aug. 15 | Aug. 28 | 13 days | 31·5 |
| Kitten 23 | Aug. 15 | Aug. 28 | 13 days | 36·5 |
| Kitten 24 | Aug. 15 | Aug. 30 | 15 days | 35·8 |

Average duration of experiment, 11·7 days.
Average loss in weight, 33·4 per cent.

The next experiment was with sterilized modified milk inoculated with a mixed culture of the *Bacillus subtilis* and the *Bacillus mesentericus vulgatus*.

### Experiment VII.

Four kittens fed on sterilized modified milk inoculated with the *Bacillus subtilis* and the *Bacillus mesentericus vulgatus* and incubated for twenty-four hours at 85° F.

Kittens numbered 25 to 28. Experiment begun August 26. Experiment ended (death of last surviving kitten) September 3.

*Kitten* 25.—The dejections were normal on the 26th and 27th. On the 28th the kitten was weak and looked ill. The dejections were firm and yellow in colour. During the day the animal became very weak and ill. The eyes were dull, and there was slight tremor of the whole body. On the 29th the dejections were paste-like in consistence, greyish in colour. The animal was collapsed, and there was marked tremor of the whole body. The animal was comatose in the evening. It died at 9 a.m. on August 30.

The kitten weighed 14 ounces at the beginning of the experiment, and 12 ounces at the end—a loss of 14·2 per cent.

*Kitten* 26.—On August 26 the dejections were normal. On August 28 and on August 29 there was no action. On the latter day the kitten looked ill and weak. On August 30 the constipation continued, the animal was ill, there was great weakness, and the eyes were dull. During the day the illness increased, the animal became very collapsed, there was marked tremor of the whole body. The kitten was too ill

to take any food after its first feed in the morning. On August 31 the animal was moribund, and the tremor was very marked. During the day it passed a very firm and dark greenish dejection. It then became comatose, and died at 7.30 p.m.

The kitten weighed 16 ounces at the beginning of the experiment, and 12½ ounces at the end—a loss of 21·8 per cent.

*Kitten* 27.—The dejections remained normal till August 29, when they became firm and greyish in colour. On August 30 there was no action, and the kitten was ill and weak, the eyes being dull. On August 31 there was no action. In the morning the kitten was in the same condition as on the previous day, but during the day it improved considerably, becoming brighter and more active. On September 1 the dejections were dark greyish in colour, and rather firm. During the day the kitten became ill. On September 2 there was no intestinal action. The animal was ill, the eyes were dull, and there was slight tremor of the whole body. During the day these symptoms increased, and in the evening the animal was comatose. It died during the night (September 3).

The kitten weighed 17 ounces at the beginning of the experiment, and 13 ounces at the end—a loss of 23·5 per cent.

*Kitten* 28.—The dejections remained normal till August 25, when they became paste-like and greyish in colour. On August 30 and 31 there was no intestinal action. On September 1 the dejections were very firm and brown in colour. On September 2 there was no action. The kitten was weak. During the day it became very collapsed, with well-marked

tremor of the whole body. The eyes were very dull. Shortly before death there was a dejection, which was very firm and almost black in colour. The kitten died during the early hours of September 3.

The kitten weighed 18 ounces at the beginning of the experiment, and $14\frac{1}{2}$ ounces at the end—a loss of 19·4 per cent.

Experiment VII.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 25 | Aug. 26 | Aug. 30 | 4 days | 14·2 |
| Kitten 26 | Aug. 26 | Aug. 31 | 5 days | 21·8 |
| Kitten 27 | Aug. 26 | Sept. 3 | 8 days | 23·5 |
| Kitten 28 | Aug. 26 | Sept. 3 | 8 days | 19·4 |

Average duration of experiment, 6·25 days.
Average loss in weight, 19·7 per cent.

The next experiment was a repetition of Experiment II. as regards the organism with which the milk was inoculated, but instead of whole cow's milk, sterilized, being employed, sterilized modified milk of the composition already given was employed.

## Experiment VIII.

Four kittens fed on sterilized modified milk inoculated with the *Bacillus subtilis* and incubated for twenty-four hours at 85° F.

Kittens numbered 29 to 32. Experiment begun September 2. Experiment ended (death of last surviving kitten) September 9.

*Kitten* 29. — The dejections were normal until September 6, when they became greyish in colour. On September 7 the animal was weak and ill, and these conditions increased during the day. From this

date the dejections remained of the same character till the 9th, when the animal died. On the morning of September 8 the kitten was very ill, the eyes were dull, and there was tremor of the whole body. During the day this tremor greatly increased, and in the evening the animal was collapsed and comatose. It died during the night.

The kitten weighed 18½ ounces at the beginning of the experiment, and 13½ ounces at the end—a loss of 27 per cent.

*Kitten* 30. — The dejections were normal till September 7. On September 6 the kitten appeared ill and weak. On September 7 there was marked diarrhœa; the dejections were very watery, pale yellow in colour, and frequent. The kitten was very ill, the eyes were dull, and there was tremor of the whole body, which increased during the day. The animal died during the night.

The kitten weighed 18 ounces at the beginning of the experiment, and 13 ounces at the end—a loss of 27·7 per cent.

*Kitten* 31.—The dejections were normal on September 2. On September 3 they were greyish and pasty. The animal rapidly became very ill, the eyes were dull, and tremor of the whole body was marked. During the day the illness increased, and in the evening the animal was collapsed and comatose. It died during the early hours of September 4.

The kitten weighed 12½ ounces at the beginning of the experiment, and 11½ ounces at the end—a loss of 8 per cent.

*Kitten* 32.—The dejections were normal on September 2. On September 3 they were paste-like and

yellow. During the day the animal became collapsed, with dulness of the eyes and general tremor. On September 4 there was diarrhœa, the dejections were very watery, greyish in colour, and contained a little blood. The animal became comatose during the day, and died in the night.

It weighed 17 ounces at the beginning of the experiment, and 14½ ounces at the end—a loss of 14·7 per cent.

Experiment VIII.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 29 ... | Sept. 2 ... | Sept. 9 ... | 7 days ... | 27·0 |
| Kitten 30 ... | Sept. 2 ... | Sept. 8 ... | 6 days ... | 27·7 |
| Kitten 31 ... | Sept. 2 ... | Sept. 4 ... | 2 days ... | 8·0 |
| Kitten 32 ... | Sept. 2 ... | Sept. 5 ... | 3 days ... | 14·7 |

Average duration of experiment, 4·5 days.
Average loss in weight, 19·3 per cent.

Up to this point all the experiments with inoculated milks had been conducted with organisms always found in milk. The next experiment was carried out with an organism which is a common and extremely powerful agent of putrefaction, and which is found in the intestine in normal circumstances—the *Bacillus proteus vulgaris*. It is, however, not commonly found in milk; and further, it is very uncommon to find it on plates exposed to the air.

## Experiment IX.

Four kittens fed on sterilized modified milk inoculated with the *Bacillus proteus vulgaris* and incubated for twenty-four hours at 85° F.

Kittens numbered 33 to 36. Experiment begun

September 5. Experiment ended (death of last surviving kitten) September 21.

*Kitten* 33.—The dejections were normal on the first day. On September 6 they were of fairly normal consistence and colour, but rather greyish. On September 7 there was no action. On September 8 the dejections were very firm, and brown in colour. The same condition obtained on the 9th. On the 10th and 11th there was no action. The kitten was ill on the 18th, there being marked weakness, and the eyes were dull. During the day the kitten became increasingly ill, and was comatose in the evening. It died at 9 a.m. on September 12.

The animal weighed 17 ounces at the beginning of the experiment, and 14 ounces at the end—a loss of 17·6 per cent.

*Kitten* 34.—The dejections were normal on September 5. There was no action on September 6 or 7. On September 8 the dejections were rather firm, paste-like, and brown in colour. This condition obtained on the 9th, 10th, and 11th. On the 12th and 13th there was no action. On the 14th the dejections were firm and brown. On the 15th they were paste-like and yellowish. On the 16th they were of the same character. The kitten appeared weak. On the 17th the dejections were the same, and the weakness was about the same. On September 18th there was no action, and the general condition remained the same. On the 19th there was no action. The kitten was now very weak, and looked ill. There was tremor of the whole body. During the day the illness increased, and the kitten became comatose. It died during the night.

It weighed 19 ounces at the beginning of the experiment, and 13 ounces at the end—a loss of 31·5 per cent.

*Kitten* 35.—On September 5 the dejection was normal. On September 6 there was slight diarrhœa, the dejections being loose and light in colour. The same condition obtained on September 7. On September 8 the diarrhœa had ceased. The dejections were paste-like and light brown in colour. There was no change on September 9 and 10. On September 11 there was slight diarrhœa, the dejections being greyish in colour. On the 12th they were again paste-like and brown. The kitten was weak and ill. On September 13 the illness increased. There was again moderate diarrhœa, the dejections being brown in colour. On September 14 the kitten was extremely ill, and towards evening became comatose. It died on September 15 at 2 p.m.

The animal weighed 17 ounces at the beginning of the experiment, and 12½ ounces at the end—a loss of 26·4 per cent.

*Kitten* 36.—The dejections were normal on September 5. On the 6th and 7th there was no action. On the 8th the dejections were very firm and brown in colour. There was no change on the 9th. On the 10th there was slight diarrhœa, the dejections being yellow in colour. This ceased during the night, and they became paste-like and brown. This condition obtained on September 12. On September 13 there was no action, and the kitten appeared to be weak and ill. On September 14 the dejections were very firm, and dark brown. The kitten looked much brighter in the morning. The weakness reappeared during the day.

On September 15 there was no action, and the general condition was about the same. On the 16th the dejections were very firm, and brown in colour. On the 17th and 18th there was no action. During these days the kitten was not definitely ill, but was weak and dull-looking. On September 19 there was no action. The kitten was now very weak, and appeared very ill. On September 20 there was still no action, the animal was worse, and there was marked tremor of the whole body. Later in the day the kitten became comatose. It died during the night.

The animal weighed 18½ ounces at the beginning of the experiment, and 12½ ounces at the end—a loss of 32·4 per cent.

EXPERIMENT IX.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 33 | Sept. 5 | Sept. 12 | 7 days | 17·6 |
| Kitten 34 | Sept. 5 | Sept. 20 | 15 days | 31·5 |
| Kitten 35 | Sept. 5 | Sept. 15 | 10 days | 26·4 |
| Kitten 36 | Sept. 5 | Sept. 21 | 16 days | 32·4 |

Average duration of experiment, 12 days.
Average loss in weight, 26·9 per cent.

The next experiment was a repetition of Experiment I., with the exception that there was an important difference in regard to the precise temperature to which the milk was raised. Instead of the milk being raised to 200° F. (93·3° C.), it was raised to 212° F., and maintained at that temperature for three minutes.

### Experiment X.

Four kittens fed on milk maintained at 212° F. (100° C.) for three minutes, and incubated for twenty-four hours at a temperature of 85° F. (29·4° C.).

Kittens numbered 37 to 40.

*Kitten* 37.—The dejections were normal on September 5, 6, 7, and 8. On the 9th and 10th there was no action. On the 11th the dejections were firm and brown in colour. The kitten was very weak and ill. There was slight tremor. On the 12th the dejections were paste-like and brown; later in the day there was diarrhœa, the dejections being very fluid in character and brown in colour. The kitten was very ill, there was marked tremor, and the eyes were dull. The animal then became comatose. It died during the night.

It weighed 18 ounces at the beginning of the experiment, and 13½ ounces at the end—a loss of 25 per cent.

*Kitten* 38.—The dejections were normal on September 5. On the 6th there was no action. On the 7th and 8th the dejections were paste-like and light brown in colour. On September 9 there was slight diarrhœa, which was replaced later in the day by pasty dejections. The kitten appeared to be rather weak, and looked ill. On September 10 the dejections were still pasty and light yellow in colour. The eyes were dull, and the general illness had increased. During the day the kitten became comatose, and it died during the night.

The animal weighed 18 ounces at the beginning of the experiment, and 14 ounces at the end—a loss of 22·2 per cent.

*Kitten* 39.—The dejections were normal on September 5. There was no action on September 6. On the 7th they were firm and grey in colour. On the 8th they were paste-like and brown. The same condition obtained on the 9th, 10th, and 11th. On the morning of the 12th the kitten looked weak and ill. On the 13th there was no action. The illness was increased, and the eyes were dull. On the 14th there was moderate diarrhœa, the actions being very watery and pale yellow in colour. The kitten was very ill, and there was slight tremor. On the 15th there was an action, which was very firm and almost black in colour. The kitten was now in a collapsed condition, and there was marked tremor. During the day the tremor disappeared, and the animal became comatose. It died during the night.

The animal weighed 15 ounces at the beginning of the experiment, and 11½ ounces at the end—a loss of 23·3 per cent.

*Kitten* 40.—The dejections were normal on the 5th. On the 6th there was diarrhœa, the actions being very loose, and light yellow in colour. On the 7th the diarrhœa was more severe, the actions being very loose and frequent, and yellow in colour. This continued throughout the 8th. On the 9th the diarrhœa had moderated, the actions being less watery and firmer. Moderate diarrhœa, with yellow or greenish-yellow dejections, continued from this date till September 17. On the 13th the kitten was rather weak and dull-looking. It remained in this condition till the 17th, when it became much weaker, and looked very ill. On September 18 the diarrhœa ceased. The dejections were paste-like, and generally yellow in colour. The

weakness and general illness had increased. On the 19th the eyes were dull, and the animal was collapsed. There was moderate diarrhœa, the dejections being very loose, yellowish in colour, with traces of black. It died during the night.

The animal weighed 17 ounces at the beginning of the experiment, and 11 ounces at the end—a loss of 35·2 per cent.

EXPERIMENT X.

| | Experiment Begun. | Kitten Died. | Duration of Experiment. | Loss in Weight Per Cent. |
|---|---|---|---|---|
| Kitten 37 ... | Sept. 5 ... | Sept. 13 ... | 8 days ... | 25 |
| Kitten 38 ... | Sept. 5 ... | Sept. 11 ... | 6 days ... | 22·2 |
| Kitten 39 ... | Sept. 5 ... | Sept. 16 ... | 11 days ... | 23·3 |
| Kitten 40 ... | Sept. 5 ... | Sept. 20 ... | 15 days ... | 35·2 |

Average duration of experiment, 10 days.
Average loss in weight, 26·4 per cent.

All of the forty animals died from the disease, the average duration of the experiments being twelve days. The first experiment, however, failed to comply with the requirements, and the four kittens lived for 19, 29, 34, and 45 days respectively from the beginning of the experiment. If this experiment be excluded, and the average be taken from the nine experiments in which there was no contamination from any acid-forming organism, the average duration of the experiments was 9·7 days.

The most rapidly fatal mixture was the sterilized modified milk inoculated with the *Bacillus subtilis* (Experiment VIII. — average duration, 4·5 days). The next most fatal was sterilized modified milk inoculated with a mixed culture of the *Bacillus subtilis* and the *Bacillus mesentericus vulgatus* (Experi-

ment VII.—6·25 days). The third most fatal was sterilized modified milk inoculated with the *Bacillus mesentericus vulgatus* (Experiment V.—7·7 days). The fourth most fatal was sterilized whole cow's milk inoculated with the *Bacillus subtilis* (Experiment II. —8·25 days). The fifth most fatal was whole milk, boiled, and then incubated for twenty-four hours without inoculation (Experiment X.—10 days).

While these figures indicate generally the conditions most favourable to the rapid production of the disease, too much importance cannot be attached to the precise figures, since it is impossible to assess the relative resistance of the individual animals—a factor which must have played a considerable part in determining the actual time of onset and the duration of the disease. This factor is illustrated in Experiment IV.; the first two kittens died within 12 days, the third at 23 days, and the last at 29 days. On the other hand, when we take the average duration of the disease throughout the whole of the experiments, this factor is nearly eliminated, for the low resistance of one animal is compensated for by the high resistance of another.

The temperature of incubation was considerably lower than that usually employed. The putrefactive organisms grow rapidly at 100° F., but their optimum temperature is between 80° and 90° F. This, of course, has a very important bearing on the incubation of the milk carried out in the homes in the hot summer.

## IV

## On the Conditions found Post Mortem

Post-mortem examinations were made in all cases. Certain adventitious conditions need to be recorded. In four instances a tapeworm or nematodes were found in the small intestine. Kitten 13 (Experiment IV.), tapeworm in lower part of small intestine; Kitten 19 (Experiment V.), tapeworm in middle portion of small intestine; Kitten 34 (Experiment IX.), some nematodes, about two inches in length, were found in the small intestine; Kitten 39 (Experiment X.), tapeworm in the middle portion of the small intestine.

The kittens were selected with great care, in order that they should be the healthiest animals obtainable. Unless this had been done, the proportion of kittens with these parasites would probably have been much higher. In kittens tapeworms and nematodes are the rule rather than the exception, and they appear to produce but little disturbance of health. I think it will be generally agreed that the presence of these parasites could not have had any material influence on the illness or death of the animals. The elimination of these animals would make no difference to the results, and I therefore consider that it is only necessary to definitely record the cases in which the parasites were found.

In Kitten 30 (Experiment VIII.) about ten inches

of the small intestine was in a condition of semi-strangulation. It appears to have been caused by a loop of the intestine becoming nipped in a mesenteric fold in the region of the cæcum. The obstruction was not complete, but the affected portion of the intestine was distended with fluid and was inflamed. The other appearances were those generally found.

The general post-mortem appearances were as follows :

The stomach was in all cases considerably distended.

In thirty-eight out of forty cases there was marked distension of the bladder. In twelve cases the distension was extreme, the bladder reaching to the level of the umbilicus, and bulging into the flanks, while the wall was so thin that the yellow colour of the urine could readily be seen through what resembled the membrane of an egg-shell.

This condition of the bladder wall was in marked contrast to that of the contracted bladder in the normal kitten, which is remarkably dense and tough. The distension of the stomach and the distension of the bladder were the only abnormal phenomena. The peritoneum and the mesenteric glands were quite normal. The heart, lungs, liver, spleen, kidneys, and pancreas presented nothing abnormal in their appearance.

The small intestine was rather contracted, and was, consequently, somewhat narrower than is usually found in the normal animal.

On opening the stomach it immediately collapsed, the distension being due to gas. The mucous membrane was normal in appearance, and there was generally present in the stomach a small amount of

fluid, which was usually clear, at other times was slightly bile stained. In all cases the reaction of the contents of the stomach was strongly alkaline, red litmus-paper being turned a deep blue.

The small intestine was in all cases entirely devoid of food material. The mucous membrane was, as a rule, coated with a viscid dry mucus. In other cases the mucus was of a more liquid character. Save for the excess of mucus, the mucous membrane appeared to be absolutely healthy. There was no trace of ulceration or other lesion. The peritoneal surface of the intestine was smooth, and there was no evidence of hyperæmia. The contents of the small intestine were strongly alkaline when free fluid was present. In some cases the intestine was so dry that the litmus-paper had to be moistened before any reaction could be obtained. The reaction in these cases was always alkaline, but it was less marked than in the cases where fluid was present.

The large intestine usually contained pasty yellow material, which consisted of the débris of milk mixed with the bile and intestinal secretions. The contents of the large intestine were strongly alkaline. The contents were usually sufficiently solid to permit of their being removed by forceps. The material so removed was carefully examined in regard to its reaction. The interior of the masses removed was found to be strongly alkaline to litmus-paper, so that the contents of the intestine were alkaline quite apart from the reaction of the mucous membrane. (In the normal kitten examined immediately after being killed by chloroform, the contents of the small and large intestines are invariably acid, while the reaction of

the mucous membrane after being washed with distilled water is alkaline.)

I summarize the post-mortem conditions found :

1. The stomach was distended with gas, and contained a small amount of fluid strongly alkaline in reaction.

2. The small intestine was contracted, entirely devoid of food material, and contained a considerable quantity of mucus. There was no ulceration and no evidence of inflammation. The contents of the small intestine were alkaline.

3. The large intestine usually contained pasty yellow material, which was strongly alkaline.

4. The liver, spleen, pancreas, kidneys, heart, and lungs presented nothing abnormal in their appearance.

5. Paralytic distension of the bladder was present in thirty-eight out of the forty cases.

## V

## On the Conditions of the Organs as determined by Microscopical Examination

A VERY thorough investigation was carried out, in order to determine what structural changes, if any, in the minute anatomy of the organs could be regarded as characteristic of, or peculiar to, the disease. Sections of the spleen, liver, and intestine were also prepared in each case, in order to determine the presence or absence of micro-organisms in these organs. One section of each organ was stained by Gram's method, so that Gram-positive organisms might be recognized, while another section was stained by methylene blue, in order to detect Gram-negative organisms. In no instance were any micro-organisms found. Mr. E. H. Shaw, whose experience in these matters needs no commendation from me, prepared and reported upon the whole of the sections, and I am much indebted to him for the thoroughness with which he carried out the examination of the numerous sections. The fact that he is responsible for the report upon the microscopical appearances lends it a weight which it would not possess were it based upon my own observations.

It may at once be said that very little structural change could be found, and I have abstracted in the following table all the essential details. Where no

departure from the normal could be detected, the organ is not referred to. Where the whole of the organs were normal, the animal is not referred to. This account therefore comprises all the abnormal, or possibly abnormal, features that were found.

EXPERIMENT I.

| | | |
|---|---|---|
| *Kitten* 1. | Liver. | Connective-tissue cells in some of the portal spaces well marked. |
| | Kidney. | Slight vacuolation of some of the epithelial cells in the convoluted tubules. Nuclei stain well. No round-celled infiltration. |
| | Lung. | Areas of collapse and emphysema; vessels congested. |
| *Kitten* 3. | Spleen. | Much congested. |
| | Lung. | Patch of broncho-pneumonic consolidation. |

EXPERIMENT II.

| | | |
|---|---|---|
| *Kitten* 5. | Liver. | Much congested. |
| *Kitten* 6. | Liver. | Connective tissue in portal spaces well marked. |
| *Kitten* 8. | Liver. | Much congested. |

EXPERIMENT III.

| | | |
|---|---|---|
| *Kitten* 9. | Kidney. | Some of the epithelial cells in the convoluted tubules degenerated and "broken up." |
| | Lung. | Hæmorrhage into some alveoli. Capillaries congested. Bronchi natural. |
| *Kitten* 10. | Kidney. | Capillaries of glomeruli distended with blood. |
| *Kitten* 11. | Liver. | Connective-tissue cells in portal spaces well marked. |
| *Kitten* 12. | Liver. | Small round cells in portal spaces. Connective tissue well marked. Capillaries and bloodvessels much congested. |
| | Kidney. | Tubular epithelium swollen and vacuolated; some cells show fatty degeneration. |

| | | |
|---|---|---|
| | | EXPERIMENT IV. |
| *Kitten* 14. | Liver. | Large number of spindle and round cells in portal spaces. |
| *Kitten* 15. | Liver. | Extreme congestion. |
| | Spleen. | Extreme congestion. |
| | Pancreas. | Very badly stained. No round-celled infiltration. |
| | Lung. | Area of collapse. |
| *Kitten* 16. | Liver. | Much congestion of bloodvessels and capillaries. Slight fatty degeneration of cells. |
| | Spleen. | Some congestion. |
| | | EXPERIMENT V. |
| *Kitten* 19. | Liver. | Connective-tissue cells in portal spaces well marked. |
| | Spleen. | Much congestion. |
| *Kitten* 20. | Liver. | Connective-tissue cells in portal spaces well marked. |
| | Spleen. | Much congestion. |
| | | EXPERIMENT VI. |
| *Kitten* 21. | Liver. | Connective-tissue cells in portal spaces well marked. |
| | Spleen. | Extreme congestion. |
| *Kitten* 22. | Liver. | Connective-tissue cells in portal spaces well marked. |
| | Spleen. | Much congestion. |
| *Kitten* 23. | Liver. | Connective-tissue cells in portal spaces well marked. |
| | Spleen. | Much congestion. |
| *Kitten* 24. | Spleen. | Much congestion. |
| | | EXPERIMENT VII. |
| *Kitten* 25. | Liver. | Connective-tissue cells in portal spaces extremely well marked. Many small round cells also present. |
| | Spleen. | Much congestion. |
| *Kitten* 26. | Liver. | Much congestion. Connective-tissue cells in portal spaces well marked. |
| *Kitten* 27. | Spleen. | Much congestion. |
| *Kitten* 28. | Spleen. | Much congestion. |

### Experiment VIII.

| | | |
|---|---|---|
| *Kitten* 29. | Liver. | Much congestion. |
| | Spleen. | Much congestion. |
| *Kitten* 30. | Liver. | Much congestion. |
| | Spleen. | Much congestion. |
| | Intestine. | Much congestion. Many inflammatory cells are present. (This was the case of semi-strangulation referred to in the account of the conditions found post mortem.) |
| *Kitten* 31. | Spleen. | Much congestion. |
| *Kitten* 32. | Liver. | Connective-tissue cells in portal spaces well marked. Capillaries congested. |
| | Spleen. | Much congestion. |

### Experiment IX.

| | | |
|---|---|---|
| *Kitten* 33. | Liver. | Some congestion. |
| | Spleen. | Much congestion. |
| *Kitten* 34. | Spleen. | Much congestion. |
| *Kitten* 35. | Liver. | Slight fatty degeneration of some cells. |
| | Spleen. | Congestion. |
| *Kitten* 36. | Liver. | Much congestion. |
| | Spleen. | Much congestion. |
| | Intestine. | Epithelium badly stained. |

### Experiment X.

| | | |
|---|---|---|
| *Kitten* 37. | Liver. | Connective-tissue cells in portal spaces well marked. |
| | Spleen. | Congested. |
| *Kitten* 38. | Spleen. | Much congestion. |
| *Kitten* 39. | Liver. | Much congestion. Many round cells in portal spaces. |
| | Spleen. | Cells badly stained, fibrous tissue well marked. |
| | Intestine. | Some round-celled infiltration of muscular coat. |
| *Kitten* 40. | Liver. | Congested. |
| | Spleen. | Much congested, cells badly stained. |
| | Intestine. | Epithelium badly stained. |

The pathological features revealed by microscopic examination were so few and so indefinite in regard to the cause of death that this part of the examination, by itself, throws no light on the nature of the disease, though taken in conjunction with the rest of the observations this negative evidence is of the highest value.

The question raised by the well-marked connective-tissue cells in the liver is a difficult one. The livers of several normal kittens were examined, and Mr. Shaw considers that, in all those cases where attention is drawn to the connective-tissue cells, there is a definite increase of these cells as compared with the normal specimens examined.

On the other hand, it must be pointed out that fibrous tissue in such organs as the liver and spleen is present in comparatively large amount in some animals. In the pig, for instance, the lobulation of the liver is very distinct, owing to the large amount of connective tissue. We are not in a position to decide what are the limits of normal variation in the kitten in regard to this tissue. In any case, the feature is not characteristic of the disease. An apparently exceptional amount of connective tissue in the portal spaces was found in fourteen cases. It was not found in twenty-six cases.

The other features call for no comment, since there was no pathological feature sufficiently well marked or sufficiently constant to allow of its being described as characteristic of the disease.

## VI

## On the Etiology and Pathology of the Disease as shown by (1) the Experimental Observations; (2) the Conditions found Post Mortem; (3) Microscopical Examination of the Organs

All the animals during the whole of the experiments were carefully and frequently observed by me. The attendant in charge was an extremely careful and conscientious man, and he noted in a book (a separate book being kept for each kitten) any changes in the appearance of the animals that he could detect. The striking feature in the whole of these experiments is the nature of the illness produced. The animals are fed on a milk capable of killing them in the course of about a fortnight. They receive this material for twenty-four hours. There are absolutely no signs or symptoms of illness. The kitten is taking the milk with avidity, gambolling in its cage, quite willing and ready to play with a reel of cotton—in other words, fit and well. This condition may continue for many days. The attendant then notices that the animal does not look well—"looks dull," "seems weak." Within twelve hours the kitten is seriously ill; within forty-eight hours, or thereabouts, it is dead.

All those who have studied the incidence of the disease in infants will realize how close is the corre-

spondence between these conditions and the natural history of the disease in infancy. Any explanation of the pathology of the disease which fails to account for this leading feature in its incidence must necessarily be extremely inadequate. Is the poison produced by these organisms formed in the milk outside the body, so that the animal is poisoned by these products? The answer, in the light of these experiments, is decidedly in the negative. The experimental conditions to support this hypothesis would be either (1) acute symptoms of poisoning within a few hours of receiving the milk; or (2) a gradually progressive illness. These are precisely the conditions which were not observed.

The signs of the disease were extremely constant. The eyes lost their natural lustre. Marked weakness, so that the animal could scarcely support itself on its feet, was one of the early signs. A little later, tremor of the whole body developed, and this gradually increased. It never, however, continued till death, for it was replaced by a profound stupor. The great weakness and general tremor may be illustrated by one observation: One kitten, which had been ill for about twenty-four hours, endeavoured to take its milk. It was so weak that it could hardly get to the saucer. As it placed its mouth to the milk its head sank, and its mouth and nostrils were submerged in the milk. In a moment or two it raised its head with an effort, and fell on its side.

The stupor into which the animals fell some time before death was so profound that it was extremely difficult to determine whether the animal was alive or not. I lifted one kitten by its ear from the floor

of its cage, so that the head and shoulders were raised some inches from the floor. I then released the ear. The kitten fell to the floor as an inert mass, and I was still unable to say whether it was living. Careful observation in a good light enabled me to detect slow and very shallow breathing.

No one seeing these forty animals dying from the disease could be in any doubt as to the essential cause. All the symptoms from the onset to the end pointed to one thing—a profound toxæmia, producing paresis and then paralysis, with profound narcosis as a prominent feature. In no instance was there any evidence that the animals suffered from pain. They were much too ill. Diarrhœa was an extremely variable symptom. In many cases there was alternation of diarrhœa with constipation. In Experiment VIII. there was diarrhœa, with rapid death, the average duration of the experiment being 4·5 days. In Experiment VII. there was an entire absence of diarrhœa, the average duration of the experiment being 6·25 days.

The post-mortem evidence supplies two important facts—(1) the paralysis of the bladder, which affords valuable confirmation of the nature of the poison and its action; (2) the marked alkalinity of the alimentary tract.

The microscopical evidence is striking in its confirmation of the power of the poison. It is well known that in the case of the most powerful poisons the action is too rapid to permit of changes in organic structure taking place. Fatty degeneration of the liver and other organs, for instance, is a sign which one might have expected to find, but, as Mr. Shaw has pointed out to me, it is essential for the production

of this condition that the illness shall have been of a sufficient duration.

After the most careful observation of the sections we have failed to detect any trace of micro-organisms—an extremely important point in relation to the nature of the disease and its "specific" or "infectious" character. Taking into consideration the facts as observed during life in regard to the incidence of the disease, the character of the disease when established, and the evidence derived from the post-mortem findings and the histological examinations, we are in a position to consider the actual pathological process responsible for the disease.

But, here, I must pause for a moment to consider the staining properties of the putrefactive organisms as represented by the *Bacillus subtilis* and the *Bacillus mesentericus.* These organisms are Gram-positive when they are taken from cultures in which they are actively living.

If a raw milk is allowed to "turn," these organisms will be found as well as the lactic organisms. But they have undergone a striking change in regard to their Gram-staining properties. When a film is prepared from soured milk and stained by Gram's method, the *Streptococcus lacticus* is stained a deep violet, but the *Bacillus subtilis* and the *Bacillus mesentericus* are now no longer Gram-positive. They are entirely decolorized, and are stained by the counterstain—dilute carbol fuchsin. In other words, the characteristic property of these organisms, by virtue of which their protoplasm fixes the gentian violet and iodine in a combination insoluble in 95 per cent. alcohol, is entirely lost. They have become, in fact, quite inert, if not

dead, and are merely vehicles for the spores which may develop later under more favourable conditions. Thus, when these organisms are placed in an acid medium, such as is found throughout the normal alimentary canal of the infant, they not only are unable to act, but they lose their most characteristic properties. In the healthy normal intestine they are, for all practical purposes, annihilated.

The determining point in the incidence of the disease is the failure of the stomach and the intestine to maintain the acid reaction of its contents. Directly this fails the putrefactive organisms proceed to actively live and develop in the alimentary canal. A complete revolution of the normal processes is thus attained. Being actively motile, the metabolism of these organisms is rapid and extensive, and the immediate products of their metabolic activity are absorbed from the intestine, and produce paralysis, coma, and death in the individual attacked. I have already pointed out that the toxic products are not present in the culture medium, for the proteolytic changes carried out consist of a series of stages by which protein matter is converted into soluble nitrogen containing material suitable for absorption by the vegetable kingdom. At a very early stage in the process poisonous bodies belonging to the most powerful group of poisons we know of—the alkaloids—are produced. But these, apparently, only exist in the initial stages of putrefaction, and, in the putrefactive changes occurring outside the body, are speedily decomposed into substances which exert no poisonous action.

The disease—acute intestinal toxæmia—may therefore be described as a disease directly caused by the

absorption of poisons produced by the action of certain micro-organisms whose normal function is the dissolution of dead organic material. These organisms, while always present in the healthy alimentary canal, are, under normal conditions, quite unable to carry out this function, since they are inert in an acid medium. The essential cause of the disease is the inability of the infant to protect itself from the action of these organisms, owing to its food being so altered from its normal character that the necessary supply of lactic acid cannot be maintained. As soon as this supply fails the disease arises. The disturbance involved in such a radical alteration of the normal conditions usually produces in the infant a more or less violent diarrhœa; but this diarrhœa is not an essential process of the disease, and it may be marked in the least severe cases and entirely absent in the most rapidly fatal. It is extremely important in regard to the disease that its two diagnostic features should be recognized—an alkaline reaction of the contents of the alimentary canal and toxæmia. For there are many other conditions giving rise to diarrhœa, while there is one condition which is the exact opposite of intestinal toxæmia—the diarrhœa caused by excessive production of acid. In such a condition the acidity of the intestinal contents is not lessened, but increased, and there is no toxæmia. One condition is profoundly dangerous, for it is caused by a powerful poison circulating in the blood; in the other a normal constituent of the intestinal contents is present in abnormal amount. This excess can only become dangerous if it be allowed to continue for such a long period that the continued diarrhœa produces a degree of exhaustion endangering life.

# PLATE I.

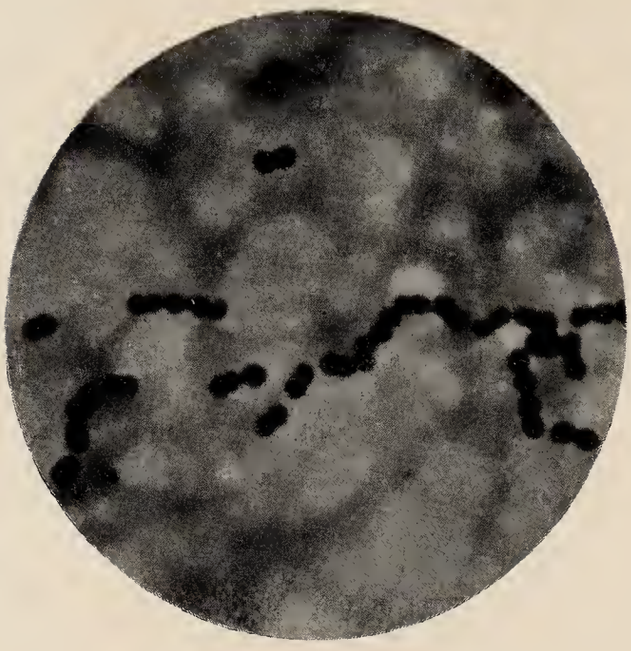


FIG. 1.—STREPTOCOCCUS LACTICUS IN MILK. (× 2,000.)

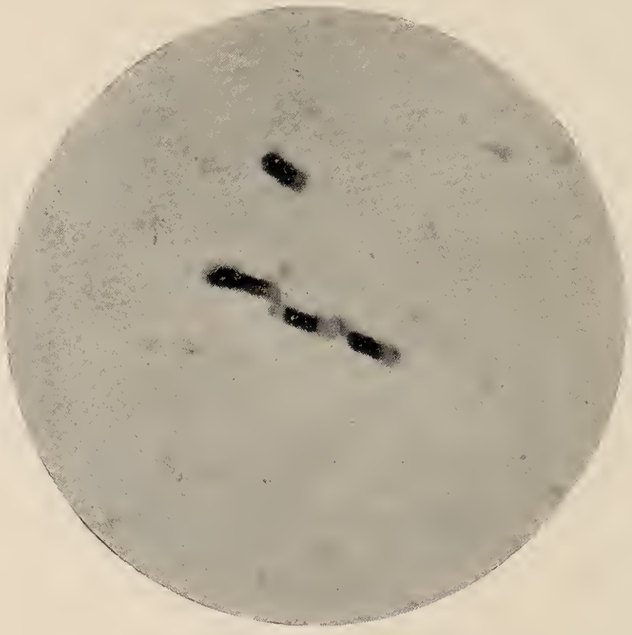


FIG. 2.—BACILLUS ACIDI LACTICI. (× 2,000.)

FIG. 3.—BACILLUS SUBTILIS. (× 2,000.)

FIG. 4.—BACILLUS SUBTILIS, SHOWING SPORES. (× 2,000.)

## VII

## On the Morphology and Cultural Characteristics of the Micro-organisms concerned in the Production of the Disease

With one exception (the *Bacillus proteus vulgaris*) the organisms have all been isolated from the milk supplied from the milk laboratory of the hospital. They have also been isolated from boiled milk, from condensed milk, and from agar plates exposed to the air in various places and circumstances.

Not being pathogenic organisms, they are not described in detail in the usual text-books; and, generally, they have received but little attention in comparison with the organisms associated with the production of specific diseases.

The terminology in regard to the putrefactive organisms leaves much to be desired. The *Bacillus subtilis*, for example, is a large bulky organism, and the term *subtilis* is therefore singularly inappropriate. The *Bacillus mesentericus vulgatus* and the other members of the "mesenteric" group are commonly found in the intestine, as, indeed, they are commonly found everywhere; but there is nothing to indicate their special connection with the intestinal canal, for, in normal circumstances, they pass through this without exerting any influence.

The *Bacillus subtilis* (Plate I., Fig. 3) is about 1 $\mu$ in

breadth, is seldom less than 2 $\mu$ in length, while it is generally from 3 to 5 $\mu$ long. It frequently grows in long chains, comprising from six to twenty organisms ; and, in old cultures, long threads may be found in which the separation between the individual rods is either very indistinct or entirely absent.

In the presence of oxygen, spore formation is extremely active. In the early stages, the spores are seen as small, round, highly refractile bodies irregularly distributed in the protoplasm of the organism. As they develop they become more or less oval in shape, and occupy the greater part of the bacillus (Plate I., Fig. 4). It is an actively motile organism, being provided with long and numerous peritrichous flagella. The single organisms move with great rapidity, while the chains of organisms move more slowly and with an eel-like movement (Plate II., Fig. 5). The spores may readily be seen in a specimen from a twenty-four hours agar-plate culture stained by Loeffler's blue. The organism is stained blue, while the spores are seen as unstained, highly refractile bodies. The *Bacillus subtilis* stains well by Gram's method.

In gelatine stab-culture the growth on the surface is a dull grey, and in from twenty-four to thirty-six hours the surface of the gelatine is liquefied. The liquefaction proceeds till the whole of the gelatine is converted into a fluid, this peptonizing action of the organism being one of its chief characteristics. It grows with extreme rapidity at 85° F. (29·4° C.), or between this and 100° F. (37·8° C.), so that an agar slant inoculated with the organism will be completely covered in twenty-four hours by an amorphous, dull,

# PLATE II.

FIG. 5.—BACILLUS SUBTILIS IN PEPTONE BROTH. (× 1,000.)
TAKEN DURING LIFE

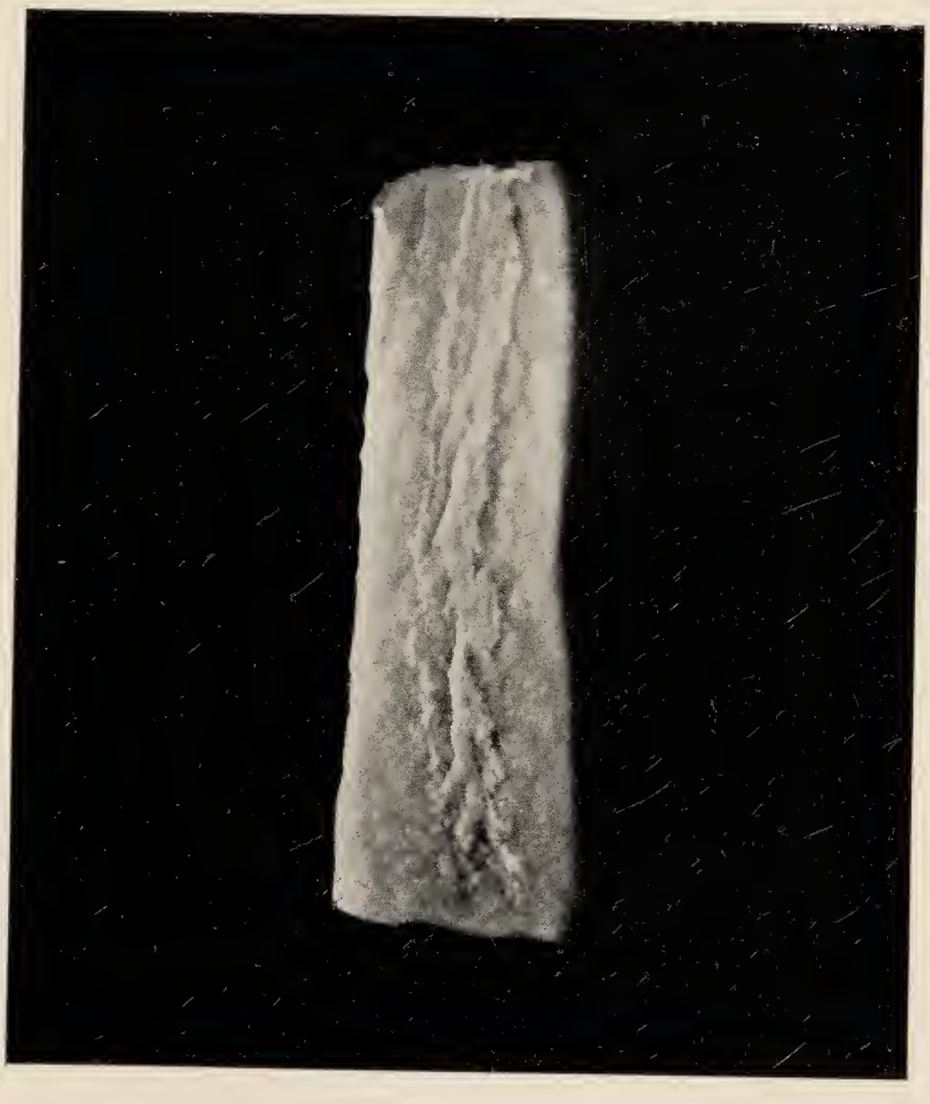


FIG. 6.—BACILLUS SUBTILIS. GROWTH ON POTATO,
TWENTY-FOUR HOURS AT 30° C.

# PLATE III.

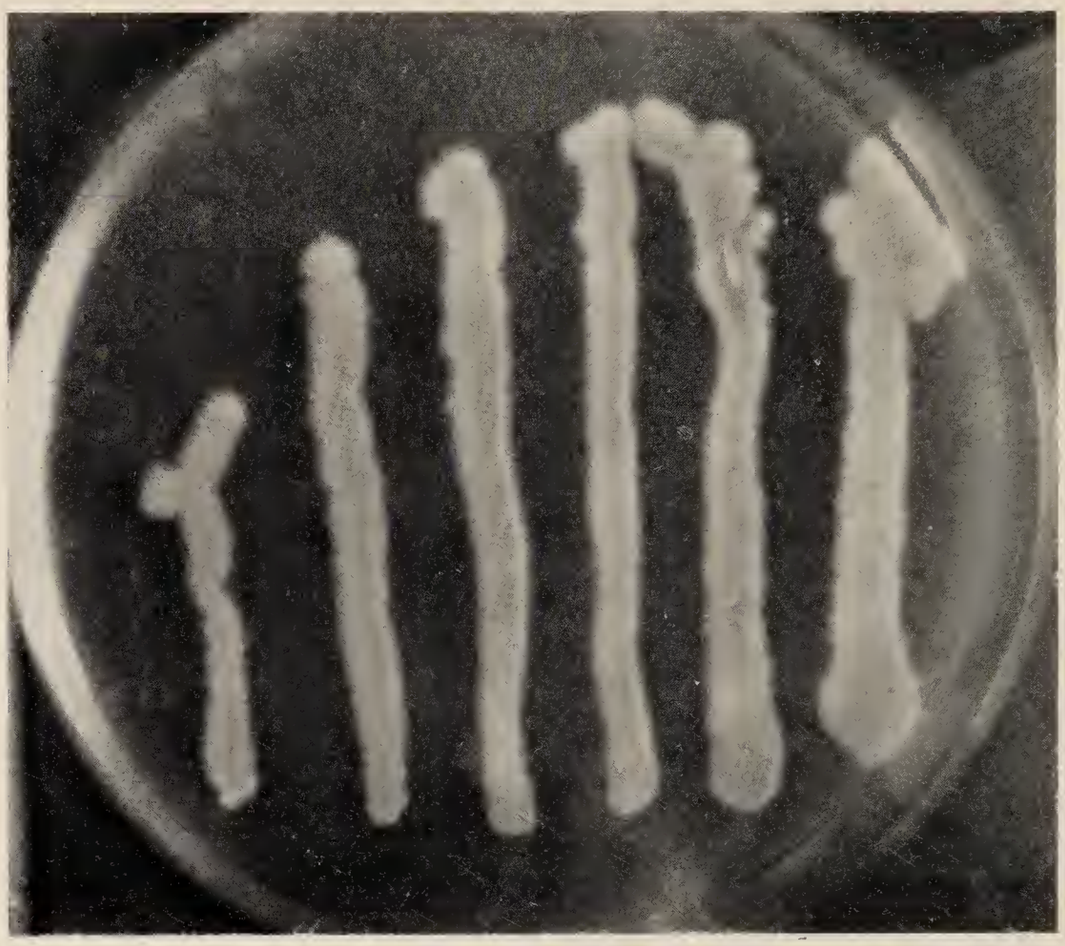


FIG. 7.—BACILLUS SUBTILIS. GROWTH ON AGAR PLATE, TWENTY-FOUR HOURS AT 30° C.

FIG. 8.—BACILLUS MESENTERICUS, "NO. 7." (× 2 000.)

yellowish-white growth. On an agar plate the growth is rather more defined (Plate III., Fig. 7).

Peptone broth is rendered turbid in twenty-four hours or less, and as the culture develops a pellicle is formed on the surface and a deposit at the bottom of the tube.

Upon potato the growth is typical (Plate II., Fig. 6). It is dull, amorphous, and not always to be readily distinguished from the surface of the potato. The dull, amorphous character of the growth on solid media is characteristic of the organism, and distinguishes it from the other varieties of putrefactive organisms.

In sterilized milk it grows rapidly, and, incubated at about 30° C., produces coagulation of the milk in from twenty-four to thirty-six hours, with a faintly alkaline reaction. As the growth proceeds, the coagulated protein is gradually taken into solution, so that in a culture of about ten days' duration the milk is converted into a brown fluid. In litmus-milk this gradual conversion may be readily seen. In a culture a few days old, the tube contains three layers. At the top is the blue litmus, freed from the milk by the coagulation. In the middle layer is a brown fluid containing the dissolved proteins, while at the bottom of the tube is the coagulated protein not yet dissolved.

The *Bacillus mesentericus* is known in the hospital laboratory as "No. 7." It undoubtedly belongs to the mesentericus group, but its cultural characters are such that it cannot at all easily be included in any of the varieties described by the authoritative writers, such as Flügge or Lehman and Neumann. For while certain features bring it under one classification, others are inconsistent with this. In these circumstances I

have preferred to leave the name of the organism an open question rather than add to the confused terminology.

The *Bacillus mesentericus* (No. 7) is a large organism from 2 to 6 $\mu$ in length, and 0·8 $\mu$ in breadth (Plate III., Fig. 8). It is frequently observed in chains and in old cultures; these chains often show little or no evidence of division into separate organisms. It is actively motile, being provided with numerous peritrichous flagella. Spore formation in the presence of oxygen is active, but there is an interesting distinction between the *Bacillus subtilis* and this organism in regard to spore formation. In a young culture the *Bacillus subtilis* is practically never found without spores. The *Bacillus mesentericus* when growing in milk or peptone broth appears to multiply chiefly by fission, for in these cultures the spores are not seen in any great number. Upon an agar plate, however, spore formation is proliferous. The spore is oval, and occupies the greater part of the organism (Plate IV., Fig. 9). The organism is Gram-positive.

In gelatine stab-culture a cloudy, funnel-shaped growth occurs in twenty-four hours. The gelatine is liquefied, and as the growth proceeds the whole of the gelatine is converted into a cloudy fluid.

In peptone broth but slight turbidity is produced, the broth remaining comparatively clear for several days. A thick greyish-white pellicle on the surface is produced in twenty-four hours at a temperature of about 30° C..

The characteristic and remarkable features of this organism are seen in its growth upon agar and upon potato. Upon an agar plate the growth is seen as

# PLATE IV.

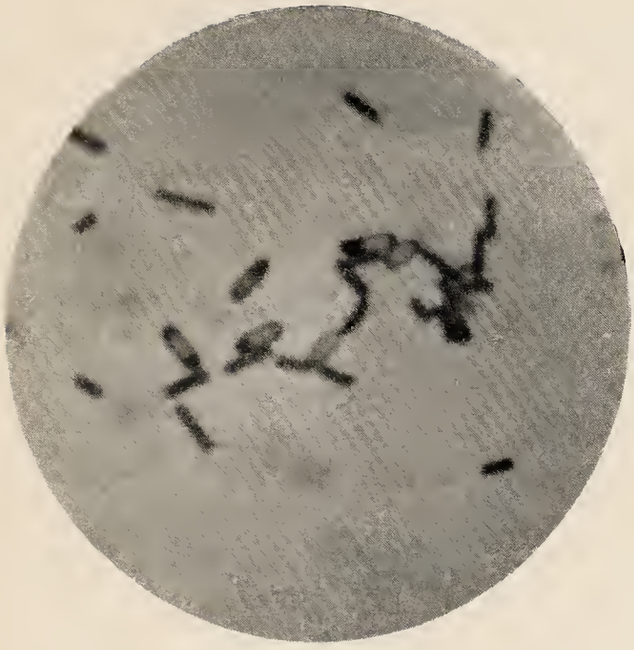


FIG. 9.—BACILLUS MESENTERICUS, "No. 7," SHOWING BACILLI AND SPORES. (× 2,000.)

FIG. 10.—BACILLUS MESENTERICUS, "No. 7," IN PEPTONE BROTH. (× 1,000.) TAKEN DURING LIFE.

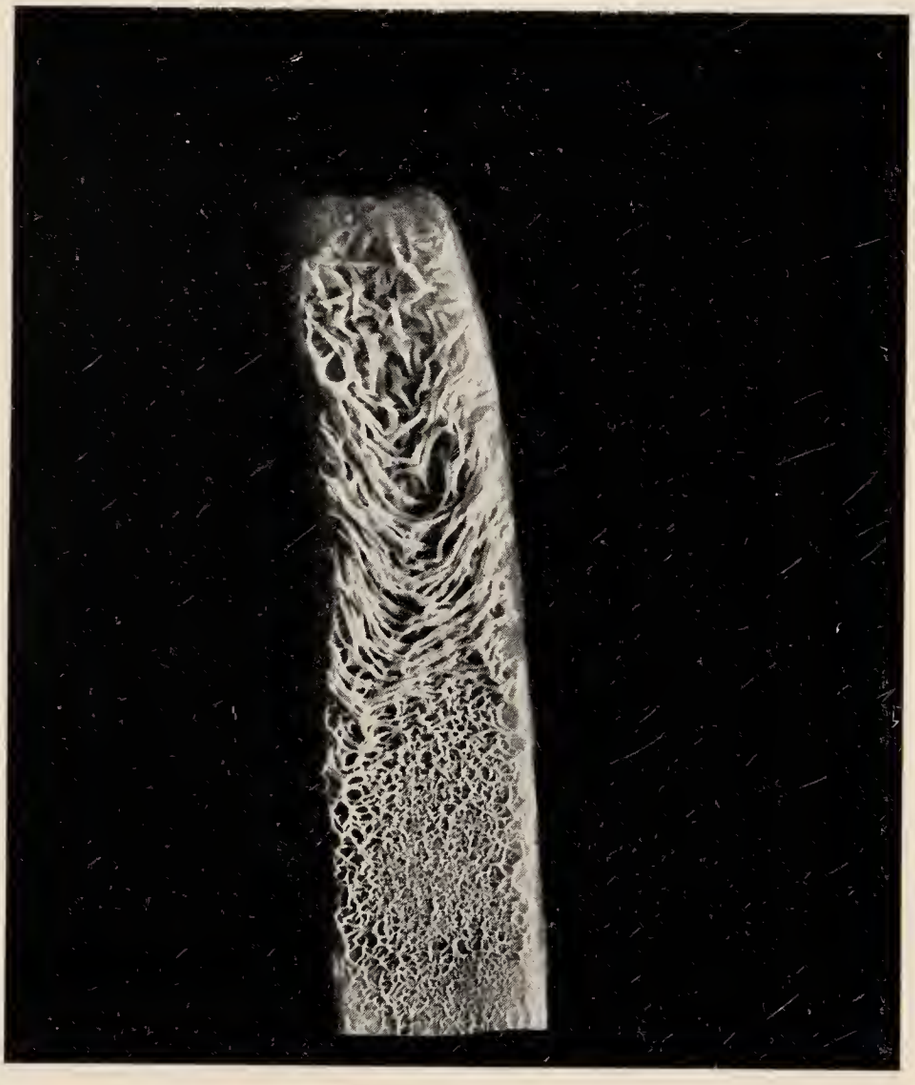


FIG. 11.—BACILLUS MESENTERICUS, "No. 7." GROWTH ON POTATO, TWENTY-FOUR HOURS AT 30° C.

# PLATE V.

FIG. 12.—BACILLUS MESENTERICUS, "NO. 7." GROWTH ON AGAR PLATE, TWENTY-FOUR HOURS AT 30° C.

a wavy, yellowish-white growth, with a scalloped edge. The rapidity and extent of the growth in twenty-four hours at 30° C. is shown in the illustration (Plate V., Fig. 12). When grown upon an agar slant, free from excess of moisture, at about 30° C., a remarkably delicate "lace and ribbon" growth is produced (Plate VI., Fig. 13).

Upon potato the growth is equally remarkable. Upon the immediate surface of the potato a delicate reticulate tissue is formed. Superimposed upon this is a luxuriant growth, consisting of ribbon-like bands, freely raised above the surface. The extraordinary rapidity and luxuriance of the growth is seen in the illustration (Plate IV., Fig. 11), which is from a photograph of a culture barely twenty-four hours old. This particular specimen was selected for illustration because it shows both the reticular and the ribbon growth. In sterilized milk the organism grows rapidly, producing coagulation at 30° C. in about twenty-four hours, with a faintly alkaline reaction.

The *Bacillus mesentericus vulgatus* is a smaller organism than those previously described, being about 0·75 $\mu$ in thickness, and from 1·5 to 3 $\mu$ in length (Plate VII., Fig. 14). It is frequently found in chains, but the bacilli forming the chains are usually quite distinct, and the long threads found in the case of the organism previously described do not occur, or are, at any rate, very uncommon. Spore formation, in the presence of oxygen, is active, the spore being single, oval in shape, and occupying the central portion of the bacillus. It is an actively motile organism, possessing numerous peritrichous flagella.

In gelatine stab-culture a greyish ragged growth,

with a fatty lustre, develops upon the surface. The growth is slower than in the organisms previously described, but there gradually develops a thick, tough membrane, which erodes the gelatine, and liquefaction of the gelatine gradually takes place.

Peptone broth is rendered slightly turbid; upon the surface and side of the tube is formed a delicate membrane, with strands. The organism does not tend at first to grow at all freely in the broth apart from the organized strands. This is so much the case that, in making a microscopic preparation from a young culture in peptone broth, it is necessary to take some portion of the membrane. If a loopful of the more or less clear broth be taken, the organisms are found to be very few in number.

Upon agar the growth is exceedingly delicate. It has a wavy, scalloped border, with a fatty lustre, and the growth is intersected at intervals by ribbon-like strands, which are considerably elevated from the surface (Plate VII., Fig. 15).

Lehman and Neumann describe the growth upon potato as exceedingly variable. I have not succeeded in getting this organism to grow upon potato. Using a culture which produces a typical growth in the other media, I have continually failed to obtain any growth on inoculating sections of potato. The action upon sterilized milk is characteristic. In contrast with the other organisms it does not produce coagulation, at any rate for a very considerable period. On the other hand, its growth is characterized by the marked production of alkalinity. Litmus-milk undergoes a typical change. The mauve or lilac tinge is completely lost, and is replaced by a Chinese blue. This feature,

# PLATE VI.

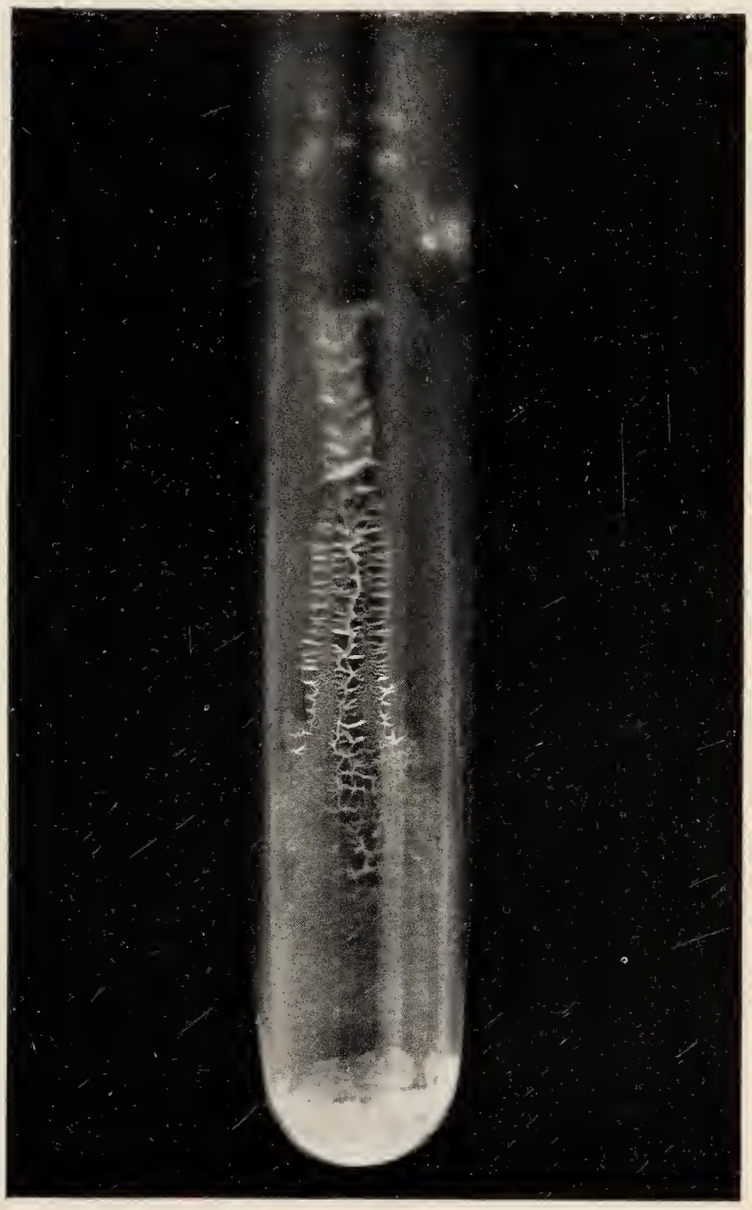


FIG. 13.—BACILLUS MESENTERICUS, "No. 7." GROWTH ON AGAR SLANT, TWENTY-FOUR HOURS AT 30° C.

# PLATE VII.

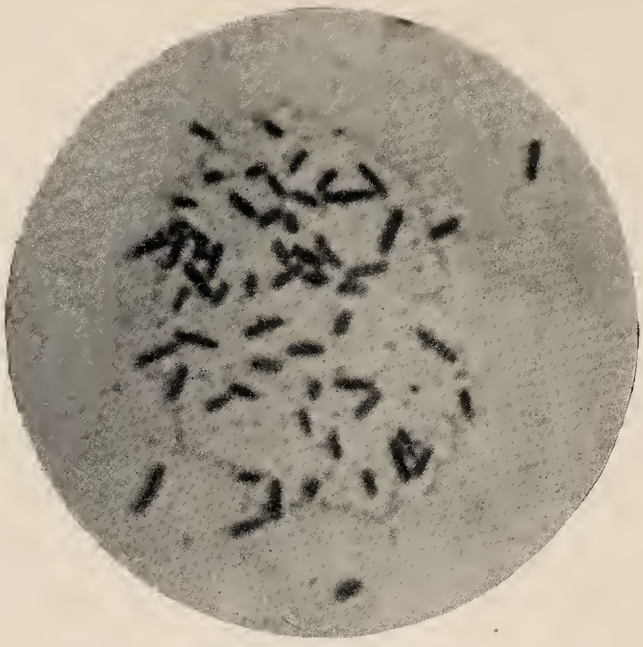


FIG. 14.—BACILLUS MESENTERICUS VULGATUS. (× 2,000.)

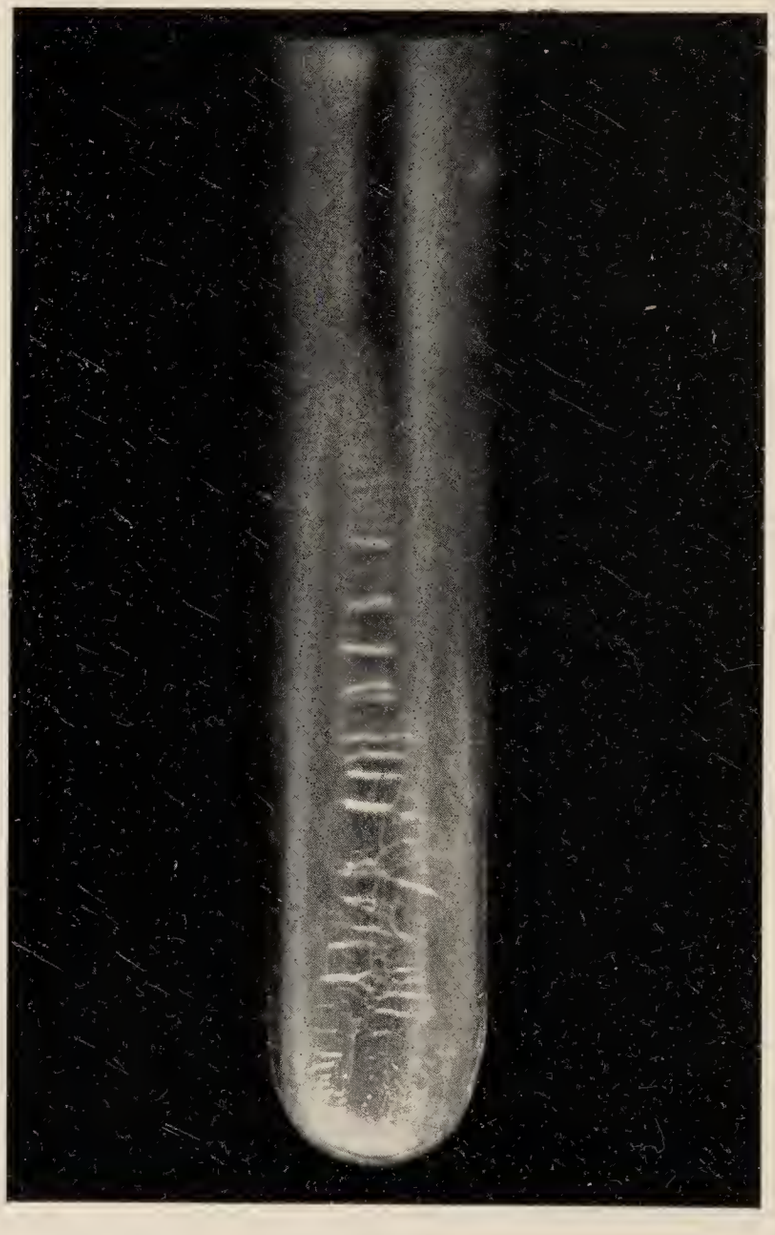


FIG. 15.—BACILLUS MESENTERICUS VULGATUS. GROWTH ON AGAR SLANT, TWENTY-FOUR HOURS AT 30° C.

together with the non-coagulation of the milk, sharply distinguishes it, in regard to its cultural characteristics, from the other organisms.

The *Bacillus proteus vulgaris* is a powerful putrefactive organism. It is readily found on the surface of meat exposed to the air, and is almost invariably present in putrefying animal matter. I have not succeeded in finding it in milk, nor have I been able to obtain it from agar plates exposed to the air. In these circumstances, it must remain an open question as to whether this organism is actually responsible for the occurrence of intestinal toxæmia in infants. There are a good many arguments against it, as will appear from the morphology and cultural characters of the organism; and, having regard to the ubiquity of such organisms as the *Bacillus subtilis* and the *Bacillus mesentericus vulgatus* and their spore formation, I think these organisms must be the agents generally acting in boiled milk. Nevertheless, the *Bacillus proteus vulgaris*, having gained access to boiled or sterilized milk, is eminently capable of producing putrefaction, and I have accordingly included it in the types of putrefactive organisms. It is a common inhabitant of the normal alimentary canal.

The *Bacillus proteus vulgaris* is from 1·5 $\mu$ to 4 $\mu$ in length, and about 0·5 $\mu$ in breadth (Plate VIII., Fig. 16). It varies very much, however, in regard to length, and has a great tendency to form involution forms, so that a single organism may be 20 $\mu$ or 30 $\mu$ in length (Plate VIII., Fig. 17). Lehman and Neumann state that this great tendency to variation is the reason for the name *Proteus*. It is actively motile, being provided with abundant peritrichous

flagella. It does not stain by Gram's method,[1] and it does not form spores. It grows extremely rapidly upon albuminous material, producing a strong alkaline reaction and a very foul odour. The gelatine stab-culture appears at first as a grey thread; at the surface rapid liquefaction takes place, which gradually invades the gelatine. Upon agar the growth is transparent and rather glistening. Peptone broth becomes extremely turbid, and there is an abundant precipitate, but no pellicle. Upon potato the growth is very indefinite and scanty. Sterilized milk is coagulated in from forty-eight to seventy-two hours, and is later rendered entirely liquid.

In selecting these organisms I have purposely selected them as types, and I do not for one moment claim that these are the only organisms capable of producing intestinal toxæmia by their action on cooked milk. The "mesentericus" group is a very large one, and there are many varieties. The two commonest organisms actually producing putrefactive changes in boiled milk are the *Bacillus subtilis* and the *Bacillus mesentericus vulgatus*. They are practically always present in the purest milk, and they may be found everywhere. They are consequently the chief representatives of this group of organisms, in reference to the putrefactive changes occurring in boiled milk.

[1] This statement applies to the organism used in my cultures. This is certainly Gram-negative. The Gram-positive or Gram-negative character of the *Proteus vulgaris* is a disputed point.

# PLATE VIII.

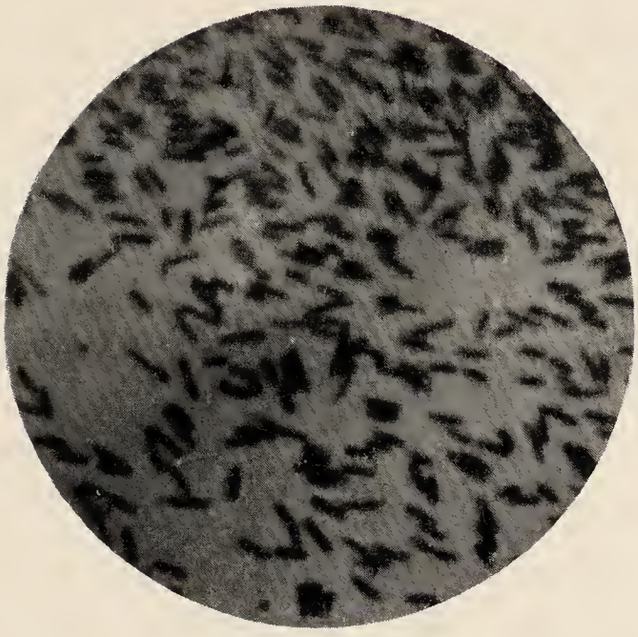


FIG. 16.—BACILLUS PROTEUS VULGARIS. (× 2,000.)

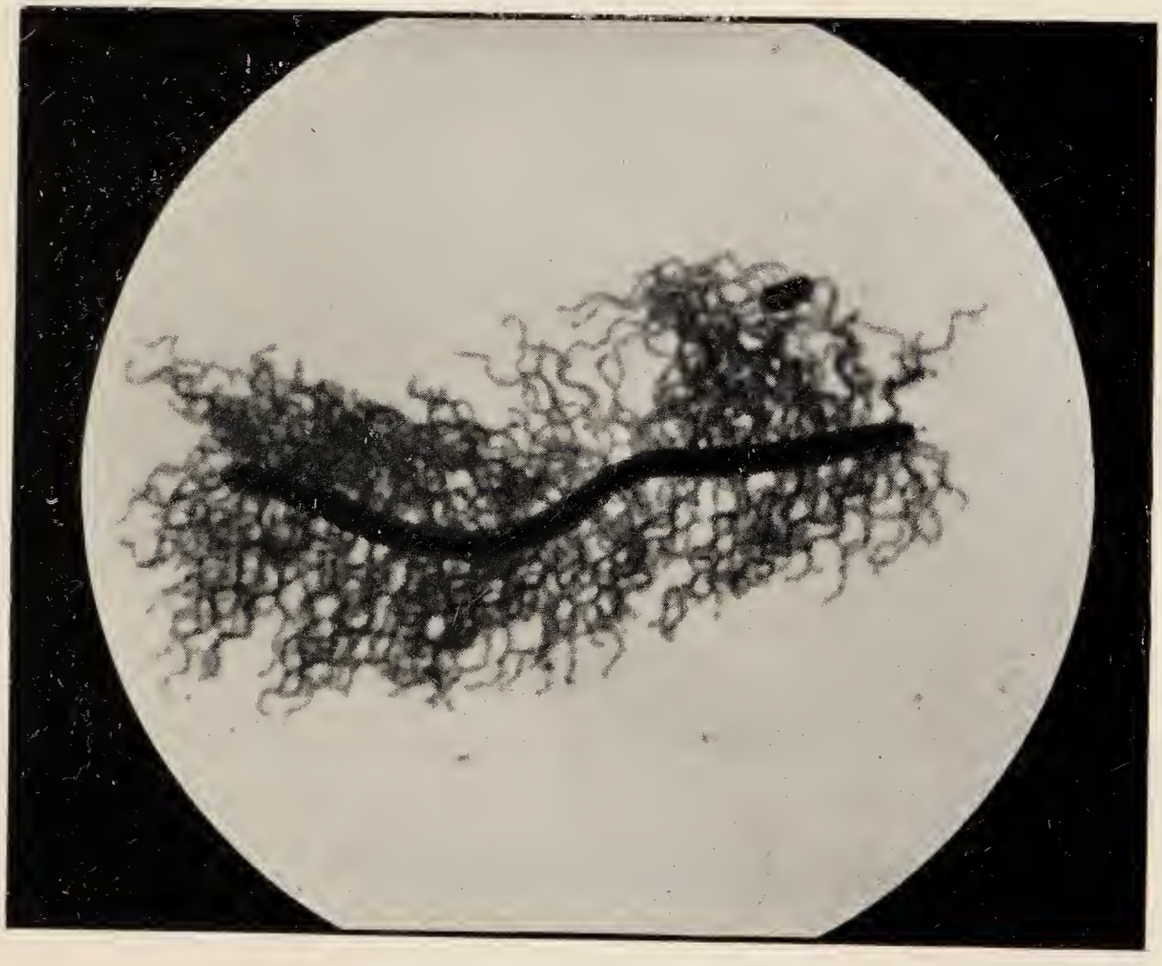


FIG. 17.—BACILLUS PROTEUS VULGARIS, SHOWING FLAGELLA. (× 2,000.)

## VIII

## On the Prevention of the Disease

The dirtier the milk, the more important is it that it should not be cooked. Boiling the milk utterly destroys the balance provided by Nature. Milk that has been boiled is not milk. The peculiar properties that characterize it and that place it in a class by itself have been destroyed. Fresh raw milk is the fundamental requirement of the infant. It is essential to its peculiar digestive and nutritive requirements.

In the out-patient department of the Infants Hospital we deal with the infants who have been discharged from the wards, and we see them at intervals of a week or a fortnight. We deal there also with infants who have not been in the hospital, but who have been brought for advice and treatment. None of these infants receive milk supplied from the hospital. Their mothers obtain it in the various districts within a ten-mile radius of the hospital. We recommend the precise milk mixture for each infant, and the mother prepares the mixture in accordance with the written directions which she receives. Every mother also receives a printed leaflet, giving certain general instructions, and one of these instructions is: "The milk *must* be fresh. It must *not* be boiled, or pasteurized, or sterilized."

We are not unaware of the dirty condition of the

milk these infants are receiving, nor unmindful of the neglect of all proper sanitary precautions which is the outstanding feature of the production and the handling of milk in this country. It is precisely because we know these things only too well that we desire to keep the milk raw. If it contains much that it ought not to contain, it at least contains also a powerful antiseptic—the *Streptococcus lacticus*. We take much care to preserve that.

But, if the feeding of infants is to be placed on a sure and efficient basis, there must be a systematic revision of the methods in which milk is handled. The most essential of all the methods required for the protection of milk are the *refrigeration of milk at the farm immediately after milking* to a temperature of 40° F. (4·3° C.) and the *transference of the milk from the farm to the town in insulated churns*. With these precautions and the delivery of the milk at the homes in the early morning and late afternoon, the milk will keep sufficiently fresh in the poorest home in the hottest weather.

It may be said that these measures are too costly, that they will inevitably raise the price of milk, and consequently will do more harm than good. I am glad to be able to show that this argument is not tenable.

The Infants Hospital is supplied with milk from its own farm. Our requirements are far more stringent than it would be advisable at present to place upon the ordinary milk vendor. The quantity of milk received *per diem* is, of course, minute when compared with the milk required by a large town. Notwithstanding the limited amount and our stringent require-

ments, this milk costs the hospital less than threepence per quart.

But there is abundant and striking evidence supplied by the milk trade itself to show that the present price of milk will easily bear the cost of refrigeration. In recent years it has, unfortunately, become the practice of large milk vendors to pasteurize the milk, while supplying it as fresh milk. Not only does this pasteurization involve considerable expense (since large quantities of milk have to be raised to a temperature of 160° or 180° F.), but there is another factor in regard to the pasteurization which is of great moment in reference to cost; for refrigerating machinery is systematically employed in conjunction with the pasteurizing machinery. The natural consequence of pasteurizing large quantities of milk is that the milk vendor has to bring this milk back again to a cool temperature. He cannot possibly effect this by means of water, and he is compelled to use refrigerating machinery in order to remove the heat from the pasteurized milk. The milk so treated is retailed at fourpence per quart, which is the ordinary price of milk. It is, therefore, obvious that the argument in relation to cost is fallacious. The milk producer and the milk vendor have to deal with an article requiring especial but easily applied precautions in regard to its handling and storage. The fishmonger and the butcher are in the same position, and, as a rule, they understand and carry out the requirements. The milk vendors ignore them.

I have dwelt upon these details because they set forth practical factors of the greatest moment. Their relation to the health of the infant is direct and

immediate. One thing else is, above all, needful—the medical profession. The younger men must go to the farm, must understand cows, must acquaint themselves with all the important factors concerned with milk production. They must be familiar with the chemistry of milk. When that is achieved they will be in a position to examine the milk their patients are receiving; they will be able to deal from exact and practical knowledge with the specious representations of the milk vendor, and the reform of the milk-supply will be gradually but surely achieved.

But it will never be achieved while we are boiling the milk. By doing this we are giving the milk vendors a full licence to be as dirty as they choose. "The doctors have discovered a patent remedy for dirt!" That is the milkman's view of the situation. It may even be said that they are growing quite enthusiastic on the subject. The systematic pasteurization of milk by the milk vendors themselves is steadily increasing. The milk is quite as dirty as it was before—it is dirtier; but the dirt is more difficult of detection, for it is rendered more obstinate and elusive.

And now I must deal as briefly as I can with the question of tuberculosis. I am compelled to discuss this, because in the letters received by me after the publication of my "Etiology of Zymotic Enteritis," in the early part of this year, one letter after another raised this question: "Is it not the fact that the scalding or pasteurizing of milk destroys the bacillus of tubercle and is to that extent beneficial? I wonder whether it is wiser to risk tubercle or to risk zymotic enteritis." This is a quotation taken at random from

one of hundreds of letters all saying the same thing in different words.

Tuberculosis attacking the infant or young child by way of the alimentary canal and through the medium of milk is, of all rare things, the rarest. It is said that the bacillus ingested with milk passes through the intact and healthy mucous membrane, and thus attacks the infant. It is an hypothesis, and an hypothesis that fails to take into account one of the most important functions of the mucous membrane of the intestine. In infancy tuberculosis is a comparatively rare disease. Hamburger investigated the question of the comparative incidence of tuberculosis in infancy and childhood, and the results of his observation were recorded in the paper read at the Conference on Tuberculosis held at Edinburgh last year. He showed that the incidence of tuberculosis in infancy is extremely infrequent as compared with childhood, and that the frequency of tuberculosis in childhood increases from year to year. The following table gives the proportions of individuals affected :

| | | |
|---|---|---|
| First year ... ... ... | 2 | per cent. |
| Second year ... ... ... | 9 | ,, |
| Third to fourth year ... ... | 27 | ,, |
| Fifth to sixth year ... ... | 51 | ,, |
| Seventh to tenth year ... ... | 71 | ,, |
| Eleventh to fourteenth year ... | 94 | ,, |

On the other hand, he found that the prognosis of tuberculosis becomes better and better according to the increasing age or incidence. In infancy tuberculosis is an acute and very fatal disease ; this is a contention which few physicians will dispute.

During the past five years I have kept careful

records of all the cases of tubercular disease in infants and young children that I have seen. I think these must be fairly representative, for the cases have occurred in all parts of the country, and I have made no selection of any kind. The one striking fact about all of them is that in not a single case was the infant or child fed on raw milk. All of them had been fed on boiled milk or on some sterilized food. Faced by such an experience as this, I am compelled to conclude that, whatever may be the means by which the infection of tuberculosis is commonly conveyed, it is certainly not by means of milk.

The one thing that impresses me in relation to tuberculosis is the enormous power of resistance to the disease in infancy and childhood. The natural history of tuberculosis in childhood is a history of malnutrition, in which the tubercle bacillus makes a tardy appearance. It is the history of an infant suffering from long-continued malnutrition. Its food has been hopelessly inadequate, and it has struggled through infancy with the signs of the struggle written upon its features and upon all its structures. The child becomes rachitic, and finally tubercular disease appears.

To produce tuberculosis in childhood, feed the babies on a cooked food. Regularly and systematically deprive the developing infant of natural food in its natural condition, and there is no scientific man who can place a limit to the consequences of such an aberration from the normal. The boiling of milk is a much more effective prescription for the production of tuberculosis than the administration of milk containing, now and again, a few tubercle bacilli; for the

healthy infant with a healthy alimentary canal will make short work of them.

I am aware that, in the expression of this opinion, I am placing a view before you which is strongly opposed by not a few physicians for whose judgment and experience I entertain unfeigned respect. But I may be allowed to remark that my observations include some thousands of infants fed on raw milk and some thousands of infants fed on cooked milk.

The physicians to whom I have alluded systematically order for the infants under their care boiled milk, and consequently they are systematically observing the abnormal. In these circumstances I do not find it a matter of surprise that the conclusions we have drawn from our observations are not in agreement.

Emmett Holt[1] writes: "Much stress has been laid upon tuberculous milk as a means by which children are affected. There is little pathological support to be found for the view that children often contract the disease in this way. In 119 autopsies upon tubercular children, chiefly infants, there was not found one in which the most advanced, and therefore presumably the primary, lesion was in the intestines or stomach. In 127 autopsies, also upon tubercular infants, Northrup found the most advanced lesion in the intestines in but a single case. While infection from milk is possible, it is certainly extremely infrequent. In my own autopsies, intestinal lesions have been found only in marked cases of generalized tuberculosis."

In a later part of his book he cites the facts in regard to a particular herd of cows in which tuberculosis affected nearly one-half of the herd:

[1] *Op. cit.*

"Near a large American city was a fancy stock farm of registered Jersey cows, which supplied milk for table use and infant feeding to a large number of families in the wealthiest part of the city for a period of over ten years. At the end of that time the tuberculin test was used for the first time, and 45 per cent. of the cows were found to be tuberculous, and were killed by order of the State Board of Health.

"The diagnosis was confirmed by autopsies upon the animals in every case. An investigation was instituted among the children who had been fed upon this milk, but in only one case of many hundreds could it be learned that tuberculosis had developed, and in this instance it was by no means established that the milk had been the source of infection.

"It should be stated that this was before the days of sterilizing milk for infant feeding. Besides the families who took the milk in the manner mentioned, the employés at the farm were accustomed to drink the skimmed milk in large quantities daily as a beverage. Many of them continued to do this for years, and yet not one of them developed tuberculosis."

We have not yet sufficiently realized that the question of the incidence of tuberculosis is a question of the resistance of the individual, and that the disease is a secondary product of ill-health and malnutrition. In regard to this, the investigation carried out by the Royal Commission on Human and Animal Tuberculosis produced some remarkable evidence, and I would invite your special attention to the records embodied in their report, for their significance can hardly be mistaken:

> "It will be understood, therefore, that we are not in a position to state absolutely what is the

minimum dose which will produce a rapidly fatal generalized progressive tuberculosis in the bovine animal when injected subcutaneously. We have no means of quantitatively appreciating the other determining factors. Our results show that with each of the strains examined, 50 milligrammes of culture, roughly calculated to contain between 200,000 and 250,000 *million* bacilli, always produce the above fatal results. Such a dose overrides everything. A dose of 10 milligrammes—*i.e.*, 40,000 to 50,000 *million* bacilli—is often fatal, but not always; this dose seems to leave room for the play of individual susceptibility. . . . In striking contrast to the ease with which, an adequate dose being used, a rapidly fatal progressive tuberculosis is set up in the bovine body by tubercle bacilli subcutaneously injected, is the difficulty of producing the same result by feeding."

In an earlier portion of the report the particulars of these experiments are given :

"In each of six cows whose udders had been made tuberculous by intramammary injection the calves were allowed to suck for varying periods, beginning the day after, or a few days after the injection. The number of bacilli ingested could not, of course, be determined. In one case only was general tuberculosis produced. In all the other five calves killed, after being kept alive from 74 to 363 days, the tuberculosis was, for the most part, limited to the intestines and mesenteric glands, a few nodules in some cases being found in the ileo-cæcal, portal, or other glands,

and in the liver or other internal organs; the lesions had the retrogressive character of being calcareous.

"Fourteen calves, varying in age from three and a half weeks to two months, were fed with tuberculous milk, six from one source, eight from another; the number of bacilli thus ingested varying from one to ten millions, and the experiments taking from 36 to 127 days. None of these calves showed, when killed, anything more than tuberculosis limited to the intestine and to the mesenteric or ileo-colic glands; in one case tuberculous lesions were found in the pharyngeal glands only.

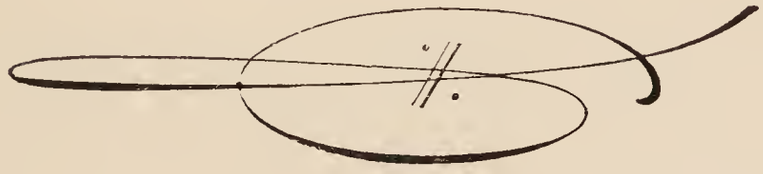
"These cases show that feeding with the bacillus of bovine tuberculosis does not so readily set up general progressive tuberculosis in the calf as does inoculation.

"Assuming that some only, and possibly few only, of the bacilli entering the mouth were absorbed by the intestine (or from the pharynx), we may attribute the smallness of the effect to the smallness of the dose actually effective. The results of feeding might then be considered as parallel to the effects of the subcutaneous injection of very small doses. Yet the calves which sucked their tuberculous mothers for many days probably ingested no inconsiderable number of bacilli (though the exact number is unknown) without producing, save in one case only, anything more than a limited and retrogressive tuberculosis."[1]

[1] Second Interim Report, 1907, pp. 10, 13.

I have dwelt upon this question of tuberculosis because I am convinced that we have paid too much attention to the bacillus and too little attention to the conditions under which it is able to attack the individual.

Which risk are we to take—tuberculosis or intestinal toxæmia? We will take neither. For so surely as we supply the infant with a food adapted to its physiological needs and adequately supplying its structural requirements, so surely shall we provide it with the most potent means of resisting the inroad of disease in all its forms.





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